L Number	Hits	Search Text	DB	Time stamp
1	7483		USPAT	2003/06/25 16:22
		564/163, 564/169, 564/170, 564/172, 562/429,		
·		562/431, 514/570, 514/571, 514/563, 514/618,		1
		514/619, 514/620, 514/621, 514/622, 514/532,		
1		514/545		
2	10647	obesity or arteriosclerosis	USPAT	2003/06/25 16:22
3	10259	thyroid\$	USPAT	2003/06/25 16:23
4	46	(560/45, 560/11, 560/17, 562/460, 564/162,	USPAT	2003/06/25 16:23
-		564/163, 564/169, 564/170, 564/172, 562/429,	l	[
		562/431, 514/570, 514/571, 514/563, 514/618,		
!		514/619, 514/620, 514/621, 514/622, 514/532,		
		514/545) and (obesity or arteriosclerosis)		ļ
		and thyroid\$		

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chain nodes :
   13 16 17
               18
                      20
                          29
                             30
                                 33
ring nodes :
                                                   42
                            10
                                    12
                                        39
                                           40
                                               41
                                11
   1 2
chain bonds :
                         9-13 10-33 11-29 12-16
                                                  16-17 17-18
                                                                18-19 18-20 35-37 38-39
             7-30 8-34
   4-38 5-13
ring bonds :
   1-2 1-6 2-3 3-4
                      4-5
                          5-6
                              7-8 7-12 8-9 9-10 10-11 11-12
                                                                39-40
                                                                       39-44 40-41
   41-42 42-43 43-44
exact/norm bonds :
                                                                             38-39
   4-38 5-13 7-30 8-34 9-13 10-33 11-29 12-16 16-17
                                                         18-19 18-20
                                                                      35-37
exact bonds : 17-18
normalized bonds:
   1-2 1-6 2-3 3-4
                     4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 39-40 39-44 40-41
   41-42 42-43 43-44
isolated ring systems :
   containing 7:39:
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Program Files\Stnexp\Queries\10082022bb.str

G1:0,S,N,CH2,CH,CF2,SO2,NH

G7:H,CN,X,Cb,Ak,CH2,CH,CF2,CF3

G5:H,Et,n-Pr,i-Pr,n-Bu,i-Bu,s-Bu,t-Bu,CH3

G4:C,S,N,CH,CF2,Ak

G2:0,S G3:0,N

G8:H,Ak

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 29:CLASS 30:CLASS 33:CLASS 34:CLASS 35:CLASS 37:CLASS 38:CLASS 39:Atom 40:Atom 42:Atom 43:Atom 44:Atom 45:CLASS

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Page 5
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L4 ANSMER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:487389 CAPLUS
DOCUMENT NUMBER: 137:57585
TITLE: Dissociated glucocorticoid receptor antagonists for the treatment of glucocorticoid associated
                                                                                                                                                                                                                    Thomson, David S.; Jennewein, Hans Michael; Pairet, Michael; Kalkbrenner, Frank; Kreideweiss, Stefan Boehringer Ingelheim Pharma Kg, Germany PCT Int. Appl., 40 pp. CODEN: PIXXD2
                side-effect
INVENTOR(S):
            PATENT ASSIGNEE(S):
SOURCE:
            DOCUMENT TYPE:
LANGUAGE:
                                                                                                                                                                                                                      Patent
English
              LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
PATENT NO. KIND DATE APPLICATION NO. DATE

MO 2002049634 A2 20020627 NO 2001-EP18839 20011215

MO 2002049634 A3 20031114

M: AE, AG, AL, AM, AT, AU, AB, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, RH, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, FR, TT, TZ, UA, UG, US, UZ, VN, YU, 2A, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RN: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZM, AT, BS, CM, CY, DE, DK, ES, FI, PR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BP, BJ, CP, CG, CI, CM, GA, GN, GO, GM, ML, MR, NE, SN, TD, TG

AU 2002019192 AS 20020701 AU 2001-29720 20011225

PRIORITY APPLM. INFO: US 2001-256876P P 20001220

MD 2001-EP14839 W 20011215

AB The invention relates to the use of glucocorticoid receptor (GR) without affecting the transrepression activity. Compde, having this profile can be used as co-medication with conventional glucocorticoids in the treatment of inflammation and immune diseases. An advantage of this combination therapy is that metabolic side-effects of glucocorticoids are antagonized and only the anti-inflammatory or anti-immune activity of the glucocorticoid in such a combination therapy, higher doses of the glucocorticoid can be used leading to better therapeutic efficacy.

I 32201-38-2, ERRS 1705E

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(dissord, Slucocorticoid receptor antagonists for treatment of glucocorticoid assocd. side-effects in relation to anti-inflammatory activity)

RN 252201-98-2 CAPUS

CN Benzeneacetic acid, 3,5-dibromo-4-{4-methoxy-2-(3-methylbenzoyl}-5-(1-methylethyl)phenoxy}- (9CI) (CA INDEX NAME)
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L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:428849 CAPLUS
DOCUMENT NUMBER: 117:5991
TITLE: Preparation of 4-phenoxyphenylacetic acids active at the glucocorticoid receptor III
INVENTOR(5): Gilner, Mikael; Hagberg, Lars; Koch, Eva; Nileson, Marita; Nu, Jinchang
PATENT ASSIGNEE(S): Karo Bio Ab, Swed.
PCT Int. Appl., 70 pp.
CODEN: PIXXD2
PATENT INFORMATION: 1
   FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                                                                                                                                                                                                           APPLICATION NO. DATE
                         PATENT NO.
                                         EBT NO. KIND DATE APPLICATION NO. DATE

2002044120 A1 20020606 W0 2001-IB2164 20011116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BF, BY, BZ, CA,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LS, LT, LU, LV, MA, MD, MG, MK, NN, MM, MX, NO, NZ,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UG, US, UZ, VN, YU, ZA, ZN, AM, AZ, BY, KG, KZ, MD, RU,
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GM, ML, MR, NE, SN,
20020121639 A5 20020611 A0 200212629 20011116
APPLN. INFO: MCCE(S): MARPAT 137:5991
                                                                                                         KIND DATE
                           WO 2002044120
                         AU 2002012629
   PRIORITY APPLN. INFO.:
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MARPAT 137:5991

OTHER SOURCE(S):

The title compds. [I, Rl = CO2H, heteroaryl; R2, R3 = H, halo, alkyl, provided that one of R2 or R3 is other than H atom; R4 = alkyl, cycloalkyl, alkenyl, alkynyl; R5 = H, alkyl, alkenyl, alkynyl; R6, R7 = aryl, heteroaryl, heterocycloalkyl) or pharmaceutically acceptable salts that are liver selective glucocriticoid receptor antagonists, and are useful in therapy and in the regulation of metab., esp. lowering blood glucose levels, were prepd. Thus, reacting 3,5-dibromo:4-[2-lhydroxy(phenyl)methyl]-5-isopropyl-4-methoxyphenoxy)phenylacetic acid with phenol in the presence of SnCl2 in CN2Cl2 afforded I (R1 = CO2H, R2, R3 = Br; R4 = iso-Pr; R5 = Me; R6 = Ph; R7 = 4-HOC6H4]. The compds. I exhibit an affinity for the glucocorticoid receptor receptor in the range between 0.1 and 5000 mM.
433685-31-29
RL: PAC (Pharmacological activity): RCT (Reactant): SPN (Syntheric

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic

ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

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ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); RACT (Reactent or reagent); USES (Usee)
(prepn. of 4-phenoxyphenylacetic acids active at the glucocorticoid
receptor III)

38868-51-2 CAPLUS
BBENZENEACETIC ACID (APLUS
BBENZENEACETIC ACID (APLUS)
BENZENEACETIC A
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Br CH2-CO2H

433686-19-2P 433686-20-5P 433686-21-6P
433686-22-7P 433686-26-1P 433686-24-9P
433686-22-7P 433686-26-1P 433686-27-2P
433686-28-3P 433686-27-9P 433686-37-0P
433686-31-8P 433686-32-9P 433686-33-0P
433686-31-1P 433686-31-5P 433686-31-0P
433686-31-4P 433686-31-5P 433686-31-0P
433686-31-4P 433686-41-0P 433686-41-0P
433686-40-3P 433686-41-0P 433686-51-4P
433686-40-3P 433686-51-4P 433686-51-4P
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433686-71-4P
433686-71-4P
43368
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(Uses)
(prepn. of 4-phenoxyphenylacetic acids active at the glucocorticoid
receptor III)
431865-19-2 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-[(4-hydroxyphenyl)phenylmethyl]-4methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

6/23/2003

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#### L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued

Ph OH Br

RN 431686-20-5 CAPLUS CN Benzeneacetic scid. 3.5-dibromo-4-[2-[(5-fluoro-2hydroxyphenyl)phenylmethyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 433686-21-6 CAPLUS

Benzeneacetic acid, 3,5-dibromo-4-[2-[(4-chloro-2-hydroxyphenyl] phenylmethyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI)
(CA INDEX NAME)

RN 433686-22-7 CAPLUS

Rn Benzeneacetic acid, 3,5-dibromo-4-[2-[(2-chloro-4-hydroxyphenyl)phenylmethyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI)
(CA INDEX NAME)

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

Benzeneacetic acid, 3,5-dibromo-4-[2-[(4,5-difluoro-2-hydroxyphenyl)]phenylmethyl]-4-methoxy-5-(1-methylethyl)phenoxy)- (9CI)
(CA INDEX NAME)

RN 433686-26-1 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-(2-[(2-hydroxy-4,5-dimthylphengyl)phenplmethyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 433686-27-2 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(2-hydroxy-5-methoxyphenyl)phenylmethyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI)
(CA INDEX NAME)

RN 433686-28-3 CAPLUS
CN Benzeneacetic acid,
-3,5-dibrono-4-[2-(1H-indol-3-ylphenylmethyl)-4-methoxyHabte

Page 6

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 433686-23-8 CAPLUS

'CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(5-chloro-2-hydroxyphenyl)phenylmethyl]-4-methoxy-5-(1-methylethyl)phenoxy)- (9CI) (CA INDEX NAME)

RN 433686-24-9 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-{(3,4-difluoro-2-hydroxyphenyl]phenylmethyl}-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI)(CA INDEX NAME)

RN 433686-25-0 CAPLUS

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued) 5-(1-methylethyl)phenoxy] - (9CI) (CA INDEX NAME)

RN 433686-29-4 CAPLUS CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(4-hydroxyphenyl)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA

RN 433686-30-7 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(3-fluoro-2-hydroxyphenyl) (3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxyl- (9CI) (CA INDEX
NAME)

### 10/082,022

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 433686-31-8 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(4-fluoro-2-hydroxyphenyl)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX

RN 433686-32-9 CAPLUS
CN Benzeneactic acid, 3,5-dibromo-4-[2-[(5-fluoro-2-hydroxyphenyl)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 433686-35-2 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(5-chloro-2-hydroxyphenyl) (3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX

RN 433686-36-3 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(3-bromo-2-hydroxyphenyl) (3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX

### Page 7

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continue

RN 433686-33-0 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(3-chloro-2-hydroxyphenyl) (3-methylphenyl) methyl}-4-methoxy-5-(1-methylethyl)phenoxyl- (9CI) (CA INDEX NAME)

RN 433686-34-1 CAPLUS
CN Benzenescetic scid, 3,5-dibromo-4-[2-[(4-chloro-2-hydroxyphenyl)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy)- (9CI) (CA INDEX
NAME)

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 433686-37-4 CAPLUS
CN Benzeneacetic acid, 3.5-dibromo-4-[2-[(4-bromo-2-hydroxyphenyl) (3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 433686-38-5 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(5-bromo-2-hydroxyphenyl)] (3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy)- (9CI) (CA INDEX

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 433686-39-6 CAPLUS

Senzeneacetic acid, 3,5-dibromo-4-[2-(2,4-dichloro-6-hydroxyphenyl) (3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxyl- (9CI) (CA

RN 433686-40-9 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-{2-[(2-hydroxy-3-methylphenyl)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxyl- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued

RN 433686-43-2 CAPLUS
CN Benzeneactic acid, 3,5-dibromo-4-{2-{(2-hydroxy-3,6-dimethylphenyl)(3-methylphenyl)methyl}-4-methoxy-5-{1-methylethyl)phenoxy}- (9CI) (CA INDEX
NAME)

RN 433686-44-3 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(2-hydroxy-4,5-dimethylphenyl)(3-methylphenyl)methyl)-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA
INDEX
NAME)

RN 433686-45-4 CAPLUS Benzeneacetic acid, 3,5-dibromo-4-[2-[(2-hydroxy-4,6-dimethylphenyl)(3-Habte

### Page 8

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 433686-41-0 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-{2-{(2-hydroxy-3,4-dimethylphenyl)(3-methylphenyl)methyl}-4-methoxy-5-{1-methylethyl}phenoxy}- (9CI) (CA
INDEX

RN 433686-42-1 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-{2-{(2-hydroxy-3,5-dimethylphenyl)}(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued) methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 433686-46-5 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(5-ethyl-2-hydroxyphenyl)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 433686-47-6 CAPLUS.
CN Benzeneacetic acid, 3,5-dibromo-4-{2-{{5-(1,1-dimethylethyl}-2-hydroxyphenyl} (3-methylphenyl)methyl}-4-methoxy-5-{1-methylethyl}phenoxy}-{5Cl} (CA INDEX NAME)

RN 433686-48-7 CAPLUS 6/23/2003 L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
CN Benzenepropanoic acid, 3-[[2-]2,6-dibromo-4-(carboxymethyl)phenoxy]-5methoxy-4-(1-methyl)phenyl](3-methyl)phenyl]+4-hydroxy-,
.alpha.-methyl ester (9C1) (CA INDEX NAME)

RN 433686-49-8 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(2,4-dihydroxyphenyl)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA

RN 433686-50-1 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[{2-hydroxy-4-methoxyphenyl) (3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued

RN 433686-54-5 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(2-hydroxy-5-(phenyl)methoxy)phenyl)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxyl-(9CI) (CA INDEX NAME)

RN 433686-55-6 CAPLUS

Renzeneacetic scid, 3,5-dibromo-4-[2-{(2-hydroxy-3-methoxy-6-methylpheny)}]

methylphenyl) (3-methylphenyl) methyl) -4-methoxy-5-(1-methylethyl)phenoxy]
(9CI) (CA INDEX NAME)

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L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 433686-52-3 CAPLUS
CN Benzeneacetic ecid, 3,5-dibromo-4-[2-[[2-hydroxy-4(trifluoromethoxy)phenyl](3-methylphenyl)methyl]-4-methoxy-5-[1methylethyl]phenoxy]- (9CI) (CA INDEX NAME)

RN 433686-53-4 CAPLUS

Senzeneacetic acid, 3,5-dibromo-4-[2-[[2-hydroxy-6-[trifluoromethoxy] phenyl][3-methylphenyl]methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 433686-56-7 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(2-hydroxy-3,4-dimethoxyphenyl)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy)- (9CI) (CA INDEX

RN 433686-57-8 CAPLUS
CN Benzeneacetic acid, 3.5-dibromo-4-{2-{(2-hydroxy-4,6-dimethoxyphenyl)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy)- (9CI) (CA INDEX

RN 433686-58-9 CAPLUS CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(6-hydroxy-2,3,4-trimethoxyphenyl)(3-6/23/2003 L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued) methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy}- (9CI) (CA INDEX

433686-59-0 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-[(6-hydroxy-1,3-benzodioxol-5-yl) (3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy)- (9CI) (CA

433686-60-3 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-[(5-hydroxy-1,3-benzodioxol-4-y1)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX

ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

433686-63-6 CAPLUS
Benzeneacetic acid, 3.5-dibromo-4-[2-[[2-hydroxy-5-(1H-pyrrol-1-yl)phenyl](3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxyl-(SCI) (CA INDEX NAME)

433686-64-7 CAPLUS
Benzeneacetic acid, 4-[2-{(3-amino-2-hydroxy-1-naphthalenyl)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxyj-3,5-dibromo-(9CI) (CA INDEX NAME)

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ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS

433686-61-4 CAPLUS
Benzeneacetic acid, 3.5-dibromo-4-[2-[(2,4-dimethoxyphenyl])(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA

433686-62-5 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-{{4-(dimethylamino)phenyl}, (3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME

433686-67-0 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-{2-[(5-bromo-1H-indol-3-y1)(3-methylphenyl)-4-methoxy-5-(1-methylethyl)phenoxyl- (9C1) (CA INDEX NAME)

433686-69-2 CAPLUS

Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-[(1-methyl-1H-indol-3-yl)(3-methylphenyl)methyl]phenoxyl- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 433686-70-5 CAPLUS
CN 1H-Indole-4-carboxylic acid,
3-[12-[2,6-dibromo-4-(carboxymethyl)phenoxy]5-methoxy-4-(1-methylethyl)phenyl](1-methylphenyl)methyll-, 4-methyleater

(9CI) (CA INDEX NAME)

RN 433686-71-6 CAPLUS
CN 1H-Indole-5-carboxylic acid,
3-[2-[2,6-dibromo-4-(carboxymethyl)phenoxy]5-methoxy-4-(1-methylethyl)phenyl)(3-methylphenyl)methyl]-, 5-methyl (9CI) (CA INDEX NAME)

ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

433686-74-9 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-(2-[(3,5-dimethylphenyl) (5-fluoro-2-hydroxyphenyl)methyl)-4-methoxy-5-(1-methylethyl)phenoxyl- (9CI) (CAINDEX NAME)

433686-75-0 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-[(4-bromo-2-hydroxyphenyl)(3-methylphenyl)methyl]-5-(1,1-dimethylethyl)-4-methoxyphenoxyl- (9CI) (CA INDEX NAME)

Page 11

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

433686-72-7 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-{(3-methylphenyl)-2-thienylmethyl]phenoxy]- (9CI) (CA INDEX NAME)

433686-73-8 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-[(3,5-dimethylphenyl)(4-hydroxyphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 433686-76-1 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-{2-{(2-bromo-4-hydroxypheny1) (3-methylpheny1)methyl}-5-(1,1-dimethylethyl)-4-methoxyphenoxy}- (9CI) (CA INDEX NAME)

433686-77-2 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-[(2-bromo-6-hydroxyphenyl)(3-methylphenyl)methyl]-5-(1,1-dimethylethyl)-4-methoxyphenoxy]- (9CI)
INDEX NAME)

RN 433686-78-3 CAPLUS
CN Benzeneacetic acid,
3,5-dibromo-4-[5-(1,1-dimethylethyl)-2-[(2-hydroxy-4,6-6/23/2003

ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued) dimethylphenyl)(3-methylphenyl)methyl]-4-methoxyphenoxy]- (9CI) (CA

433686-79-4 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-(5-{1,1-dimethylethyl}-2-{(2-hydroxy-3-methoxy-6-methylphenyl}(3-methylphenyl)methyl]-4-methoxyphenoxy)- (9CI)
(CA INDEX NAME)

433686-80-7 CAPLUS

Benzeneacetic acid,
-dibromo-4-[5-cyclopenty1-2-[(2-hydroxy-3-methoxy-5-methylphenyl)(3-methylphenyl)methyl)-4-methoxyphenoxy)- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued) methylphenyl)methyl]-4-hydroxy-5-(1-methylethyl)phenoxy)- (9CI) (CA INDEX NAME)

348166-50-7 348166-93-8 433686-84-1
433686-85-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of 4-phenoxyphenylacetic acids active at the glucocorticoid receptor III)
388166-50-7 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-[hydroxy(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

348166-93-8 CAPLUS
Benzeneacetic acid,
dibromo-4-{2-{3,5-dimethylphenyl}hydroxymethyl}-4methoxy-5-(1-methylethyl)phenoxy}- (9C1) (CA INDEX NAME)

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L4 'ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS

433686-81-8 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-(2-(diphenylmethyl))-4-methoxy-5-(1-methylathyl)phenoxy)- (9CI) (CA INDEX NAME)

433686-82-9 CAPLUS

Benzeneacetic acid, 3,5-dibromo-4-[2-[1H-imidazol-1-yl(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

433686-83-0 CAPLUS Benzeneacetic acid, 3,5-dibromo-4-[2-[(2,5-dihydroxyphenyl)(3-

ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS

433686-84-1 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-(5-(1,1-dimethylethyl)-2-(hydroxy(3-methylphenyl)methyl)-4-methoxyphenoxy)- (SCI) (CA INDEX NAME)

RN 433686-85-2 CAPLUS
CN Benzeneacetic acid,
3,5-dibromo-4-[5-cyclopentyl-2-(hydroxyphenylmethyl)-4methoxyphenoxy)- (9C1) (CA INDEX NAME)

252043-61-1P 348166-39-2P 348166-62-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. of 4-phenoxyphenylacetic acids active at the glucocorticoid receptor III) 252043-61-1 CAPLUS
Benzeneacetic acid, 4-{2-benzoyl-4-methoxy-5-(1-methylethyl)phenoxy}-3,5-

6/23/2003

ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued) dibromo-, methyl ester (9CI) (CA INDEX NAME)

RN 348166-39-2 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono-4-[2-(hydroxyphenylmethyl)-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

348186-62-1 CAPLOS Benzeneacetic acid, 3,5-dibromo-4-[2-[chloro(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 3 OP 6 CAPLUS COPYRIGHT 2003 ACS (Continued) and in the regulation of metab., esp. lowering blood glucose levels, were prepd. E.g., a multi-step synthesis of I [R1 = CO2H; R2, R3 = Br; R4 = iso-Pr; R5 = (CH2)2C:(CH2)Me; X = CO; R6 = 3-MeC6H4] was given. The compds. I exhibit an affinity for the glucocorticoid receptor in the

compds. I exhibit an affinity for the glucocorticoid receptor in the process of the composition of the compo

434327-07-8 CAPLUS Benzeneacetic acid, dibromo-4-[2-(3-methylbenzoyl)-5-(1-methylethyl)-4-(2-propynyloxy)phenoxyl- (9CI) (CA INDEX NAME)

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### Page 13

L4 ANSWER 3 OF 6
ACCESSION NUMBER:
DOCUMENT NUMBER:
INVENTOR(S):
PATENT ASSIGNEE(S):
SOURCE:
DOCUMENT TYPE:
LANGUAGE:
PATENT ACC. NUM. COUNT:

DOCUMENT COUNTS

COPPRIGHT 2003 ACS
ACCESSION CAPLUS
2002-428637 CAPLUS
137:02230
Preparation of 4-phenoxyphenylacetic acids active at the glucocorticoid receptor II
Peleman, Benjamin; Gustafeson, Annika; Kym, Philip R.
Karo Bio AB, Swed.; Abbot Laboratories
PCT Int. Appl., 41 pp.
CODEN: PIXXD2
PATENT
PATE

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

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			LT	, LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,
			RU	, SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	υz,
			VN	, YU,	ZA,	ZW,	AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM			
		RW	: GH	, GM,	KΕ,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AT,	BE,	CH,
			CY	, DE,	DK,	ES,	PI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,
			BF	, BJ,	CF.	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
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										WO 2	001-	<b>IB23</b>	02	W	2001	1128		
						MAR	200	1 2 7 .	2022	^								

The title compds. [I; X = CH2, CHYR7, CHYCOR7, CO, CS, C:NOR8; Y = O, S, NR8; R1 = CO2H, heteroaryl; R2, R3 = H, halo, alkyl, provided that one of R2 or R3 is other than hydrogen; R4 = alkyl, alkenyl, alkynyl, halo,

R5 = alkyl which is substituted by A (provided that A is not halo),

alky1,
 alkeny1, etc.; R6 = alky1, cycloalky1, heterocycloalky1, etc.; R7 = H; R8
 = H, alky1, cycloalky1, etc.; A = halo, cycloalky1, alkeny1, etc.] that
 are liver selective glucocorticoid receptor antagonists, useful in
therapy

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS

434327-08-9 CAPLUS

CN Benzeneacetic acid,
3,5-dibromo-4-[2-(3-methylbenzoyl)-5-(1-methylethyl)-4(3-pentynyloxy)phenoxy]- (9CI) (CA INDEX NAME)

RN 434327-09-0 CAPLUS
CN Benzeneacetic acid,
3,5-dibromo-4-{4-(a-methoxyethoxy)-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxyl- (9CI) (CA INDEX NAME)

434327-10-3 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-(4-[2-(2-methoxyethoxy)ethoxy]-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxyl - (9CI) (CA INDEX NAME)

6/23/2003

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

434327-11-4 CAPLUS
Benseneacetic acid,
-dibromo-4-(4-[2-[2-(2-methoxyethoxy)ethoxy]2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

PAGE 1-A

— co2H

434327-12-5 CAPLUS Benzeneacetic acid. 3,5-dibromo-4-[4-[(7-hydroxyheptyl)oxy]-2-(3-methylbenzyl)-5-(1-methylathyl)phenoxyl- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 434327-16-9 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono-4-[2-(3-methylbenzoyi)-5-(1-methylethyl)-4(phenylmethoxy)phenoxy)- (9CI) (CA INDEX NAME)

434327-17-0 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-[(2-fluorophenyl)methoxy]-2-(3-methylbenzyl)-5-[1-methylethyl)phenoxy]- (9Cl) (CA INDEX NAME)

Page 14

ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS

434327-13-6 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-[2-(ethylthio)ethoxy]-2-[3-methylbenzoy]-5-[1-methylethyl]phenoxy]- (SCI) (CA INDEX NAME)

434327-14-7 CAPLUS
Benzeneacetic acid, 4-[2-benzoyl-4-(carboxymethoxy)-5-(1-methylethyl)phenoxy)-3,5-dibromo- (9CI) (CA INDEX NAME)

434327-15-8 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-[(5-carboxypenty1)oxy]-2-(3-methy1benzoy1)-5-(1-methy1ethy1)phenoxy]- (9CI) (CA INDEX NAME)

ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS

434327-18-1 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-[(3-fluorophenyl)methoxy]-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxyl-\_(9CI) (CA INDEX NAME)

434327-19-2 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-[(4-fluorophenyl)methoxy]-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 434327-20-5 CAPLUS

Senzenescetic acid,
3,5-dibromo-4-(2-(3-methylbenzoyl)-5-(1-methylethyl)-4((3-methylphenyl)methoxylphenoxyl- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

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434327-23-8 CAPLUS
Benzeneacetic acid,
-dipromo-4-[2-(3-methylbenzoyl)-5-(1-methylethyl)-4[{3-nitrophenyl)methoxy]phenoxy]- (9CI) (CA INDEX NAME)

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ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

434327-21-6 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-[4-(1,1-dimethylethyl)phenyl]methoxy)-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxyl-(9CI) (CA INDEX NAME)

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RN 434327-22-7 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono-4-[2-(3-methylbenzoyl)-5-(1-methylethyl)-4[[4-(trifluoromethoxy)phenyl]methoxy]phenoxy]- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

434327-24-9 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-{4-((4-carboxyphenyl)methoxy]-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

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L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS

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PAGE 2-A

RN 434327-25-0 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono 4-[4-[4-(methoxycarbonyl)phenyl]methoxyl2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxyl- (9CI) (CA INDEX NAME)

PAGE 1-A

434327-26-1 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-{4-[(3,5-difluorophenyl)methoxy]-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxy)- (9CI) (CA INDEX NAME)

ANSMER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
Benzeneacetic acid, 3,5-dibromo-4-[4-[(6-chloro-1,3-benzodioxol-5yl]methoxy]-2(3-methylbenzoyl)-5-(1-methylethyl)phenoxy]- (9CI) (CA
INDEX NAME)

RN 434327-29-4 CAPLUS
CN Benzeneacetic acid,
3,5-dibromo-4-[2-(3-methylbenzoyl)-5-(1-methylethyl)-4{4-pyridinylmethoxy}phenoxy]- (9CI) (CA INDEX NAME)

RN 434327-30-7 CAPLUS
CN Benzeneacetic acid,
3,5-dibrom-4-[2-(3-methylenzoyl)-5-(1-methylethyl)-4[2-(4-methyl-5-thiazolyl)ethoxy]phenoxy]- (9CI) (CA INDEX NAME)

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L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS

RN 434327-27-2 CAPLUS
CN Benzeneacetic acid,
3,5-dibromo-4-{4-{C-bromo-2-methoxyphenyl}methoxy}-2{3-methylbenzoyl}-5-(1-methylethyl)phenoxy|- {9CI} (CA INDEX NAME)

ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

434327-31-8 CAPLUS Benzeneacetic acid, -dibromo-4-[2-(3-methylbenzoyl)-5-(1-methylethyl)-4-[(3-phenyl-2-propenyl)oxy]phenoxyl- (9CI) (CA INDEX NAME)

RN 434327-32-9 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono-4-{2-(3 mechybbenzoyl)-5-(1-methylethyl)-4(4-phenylbutoxy)phenoxyl- (9Cl) (CA INDEX NAME)

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 434327-33-0 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono-4-[2-(3-methylbenzoyl)-5-(1-methylethyl)-4[2-(1-piperidinyl)ethoxy)phenoxyl- (9CI) (CA INDEX NAME)

PAGE 1-A

ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of 4-phenoxyphenylacetic acids active at the glucocorticoid
receptor II)
252043-62-2 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-(3-methylbenzoyl)-5-[1methylethyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

RN CN

252201-98-2 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-(3-methylbenzoyl)-5-(1-methylthyl)phenoxyl- (9C1) (CA TNDEX NAME)

348167-25-9 CAPLUS
Benzeneacetic acid,
3,5-dibromo-4-[4-hydroxy-2-(3-methylbenzoyl)-5-(1-methylthyllphenoxyl- (9CI) (CA INDEX NAME)

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ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS

PAGE 2-A

RN 434327-34-1 CAPLUS
CN Benzeneacetic acid,
3,5-dibromo-4-[2-(3-methylbenzoyl)-5-(1-methylethyl)-4{2-(4-morpholinyl)ethoxylphenoxyl- (9CI) (CA INDEX NAME)

PAGE 1-A

252043-62-2P 252201-98-2P 348167-25-9P 348167-27-1P

- ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
  348167-27-1 CAPLUS
  Benzeneacetic acid, 3,5-dibromo-4-[4-hydroxy-2-(3-methylebnzoyl)-5-(1-methylebnzoyl)-, methyl ester (9CI) (CA INDEX NAME)

OTHER SOURCE(S):

```
L4 ANSWER 4 OF 6, CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2001:489346 CAPLUS
                                                    135:92440
Preparation of diphenyl ethers as liver selective glucocoticoid receptor antagonists
Apelqvist, Theress; Gillner, Mikael; Gustavsson, Annika; Hagberg, Lars; Koch, Evs; Lindberg, Marita Pelcman, Benjamin; Mu, Jinchang; Kym, Philip R. Karo Bio AB, Swed; Abbott Laboratories
PCT Int. Appl., 79 pp.
CODEN: PIXXD2
Patent
English
  DOCUMENT NUMBER:
                                                      135:92440
  TITLE:
  INVENTOR(S)
  PATENT ASSIGNEE(S):
SOURCE:
  DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued) inflammation (no data). 348166-47-2P IT 34816-47-2P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SFN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(intermediate; prepn. of di-Ph ether liver selective glucocorticoid receptor antagonists starting from phenols and diphenyliodonium selts)
RN 34816-47-2 CAPUJS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(2,4-difluorophenoxy)(2-methylphenyl)methyl]-4-methoxy-5-(1-methylphenyl)methyl]-4-methoxy-5-(1-methylphenyl)methyl]-4-methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methyll-4-methoxy-5-(1-methylphenyl)methyll-4-methyll-4-methoxy-5-(1-methylphenyl)methyll-4-methyll-4-methoxy-5-(1-methylphenyl)methyll-4-meth

252043-61-1P 252043-62-2P 252201-98-2P
258819-65-7P 258819-74-8P 258820-02-9P
258820-03-0P 258820-17-6P 346166-42-7P
348166-52-0P 348166-64-1P 346166-49-4P
348166-52-9P 348166-54-1P 346166-54-1P
348166-53-9P 348166-54-1P 348166-54-1P
348166-95-0P 348166-93-4P 348167-10-0P
348167-03-1P 348167-04-4P 348167-10-2P
348167-11-3P 348167-10-64-P 348167-12-2P
348167-13-9P 348167-72-1P 348167-22-6P
348167-35-9P 348167-72-1P 348167-22-6P
348167-35-9P 348167-72-1P 348167-22-6P
348167-35-9P 348167-72-1P 348167-22-6P
348167-35-9P 348167-87-1P 348167-22-6P
348167-35-9P 348167-37-1P 348167-32-2P
348167-35-3P 348167-32-3P
348167-35-3P
348

ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

The title compds. (1) [wherein R1 = CO2H, CONHOH, COCO2H, SO3H, P(O) (OH) (OR8), P(O) (OH) (NR9R10), or (unlaubatituted heteroary); R2 and R3 = independently H, halo, (halo)atkyl, OH, (halo)atkyo, (halo)atkythio, perfluoroatkyl, or perfluoroatkoxy; R4 R5, R6, and R7 = independently (unlaubatituted (perfluoroatkyl, cycloatkyl, atkenyl, or atkynyl; or R4 and R5 = independently (unlaubatituted theterocycloatkyl or (heterolaryl; or R4, R6, and R7 = independently halo, OR8, SR8, SOR8, SOZR8, NR9R10, NR11c(Z)R8, NR11c(Z)NR9R10, NR11c(Z)NR9R10, OR81SOZR11, or NR11SOZNR9R10, or R6 and R7 = independently OC(Z)R8, OC(Z)OR8, OC(Z)NR9R10, OSOZNR9R10, NR1ISOZR8,

;
R8, R9, R10, and R11 = independently H or (un)substituted
(perfluoro)alkyl, cycloalkyl, alkenyl, alkynyl, heterocycloalkyl,
(hetero)aryl, etc.; Y = H, OH, (halo)alkoxy, perfluoroalkoxy, acyloxy,
(halo)alkylthio, perfluoroalkylthio, alkylsulfonyloxy, asido, or NR9NR10;
Z = O, S, NR8, N(NR9R10), N(OR8), NSO2NR9R10, N(CN), CH(NO2), or CR9R10;
or pharmaceutically acceptable aslts, stereoisomers, or prodrugs thereof
were prepd. as liver selective glucocorticoid receptor antagonists for

the
regulation of metab., esp. lowering blood glucose levels. For example, a
soln. of 3,5-dibrono-4-hydroxyphenylacetic acid Me ester and TEA in
CH2Cl2
was added to a mixt. of bis(3-isopropyl-4-methoxyphenyl)iodonium
tetrafluoroboxate (prepn. given) and copper bronze in CH2Cl2 to give
3,5-dibromo-4-(3-isopropyl-4-methoxyphenoxy)phenylacetic acid Me ester
(761). Conversion to the ketone via a Priedel-Crafte reaction with AcCl
(761) and redn. using NaBM# in MeOH and LiOH (911) gave II. I exhibited
affinity for the glucocorticoid receptor in the range between 0.1 and

nM. Thus, I are useful for the treatment of diseases assocd, with metab. dysfunction, such as Type I and Type II diabetes, Cushing's syndrome, and

ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

252043-62-2 CAPLUS Benzeneacetic acid, 3.5-dibromo-4-[4-methoxy-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxy)-, methyl ester (9CI) (CA INDEX NAME)

252201-98-2 CAPLUS 292201-98-2 CAPLUS Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

258819-65-7 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-(3-iodobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

i-Pr Br CH2-CO2H

RN 258819-74-8 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono-4-[2-(3,5-difluorobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

MeO Br

RN 258820-02-9 CAPLUS
CN Benzeneactic acid, 3,5-dibromo-4-[4-methoxy-2-(2-methylbenzoyl)-5-(1-methylethyllphenoxyl-, methyl ester (9CI) (CA INDEX NAME)

MeO Br

RN 258820-03-0 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-(4-methylbenzoyl)-5-(1-methylethyl)phenoxyl-, methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
methylphenyl)methyl]-5-(1-methylethyl)phenoxy)-, methyl ester (9CI) (CA
INDEX NAME)

RN 348166-46-1 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[chloro(2-methylphenyl)methyl]-4methoxy-5-(1-methylethyl)phenoxyl-, methyl ester (9C1) (CA INDEX NAME)

MeO Br CH2- C-OME

RN 348166-49-4 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylathyl)-2-[(2-methylphenyl)](2-methylpropyl)amino]methyl]phenoxy]-, methyl ester (9CI)(CA INDEX NAME)

i-Bunn-CH-Br

RN 348165-52-9 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-[methoxy(3-methylphenyl)methyl]-5-(1-methylethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

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L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

MeO Br CH2-C-OMe

RN 258820-17-6 CAPLUS
CN Benzeneacetic acid,
3,5-dibromo-4-[2-(3,5-difluorobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

MeO Br CH2-C-OMe

RN 348166-42-7 CAPLUS

Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-[[2-(methylsulfonyl)ethoxy)phenylmethyl]phenoxy]-, 2-(methylsulfonyl)ethyl
ester (9CI) (CA INDEX NAMS)

RN 348166-45-0 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-[methoxy(2-

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued

MeO Br Me

RN 348166-54-1 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-[(1-methylethoxy)(3-methylpheny)]methyl]-5-(1-methylethyl)phenoxy]-, 1-methylethyl ester
(9CI)
(CA INDEX NAME)

RN 348166-56-3 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(cyclohexyloxy)(3-methylphenyl)methyl)-4-methoxy-5-(1-methylethyl)phenoxyl-, cyclohexylester (9CI) (CA INDEX NAME)

Br Pr-1

RN 348166-65-4 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-[[1-methylethyl]amino] (3-methylphenyl)methyl]phenoxy)-, methyl ester (9CI) (CA INDEX NAME)

ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 348166-92-7 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono-4-[2-[3-(dimethylamino)benzoyl]-4-methoxy5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 348166-94-9 CAPLUS
CN Benzeneacetic acid,
3,5-dibromo-4-[2-(3,5-dimethylbenzoyl)-4-methoxy-5-(1methylethyl)phenoxyl-, methyl ester (9CI) (CA INDEX NAME)

RN 348166-95-0 CAPLUS
CN Benzeneacetic acid,
3,5-dibromo-4-[2-(3,5-dimethylbenzoyl)-4-methoxy-5-(1-

ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

348167-03-3 CAPLUS
Benzeneacetic acid,
dibromo-4-(2-(4-fluoro-3-methylbenzoyl)-4-methoxy5-(1-methylethyl)phenoxy)-, methyl ester (9CI) (CA INDEX NAME)

RN 348167-04-4 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono-4-[2-(4-fluoro-3-methylbenzoyl)-4-methoxy5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

348167-10-2 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[5-(2-cyclopentylethyl)-4-methoxy-2-(3-methylbenzoyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

Page 20

ANSMER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued) methylethyl)phenoxyl- (9CI) (CA INDEX NAME)

RN 348166-99-4 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono-4-[2-(3-chloro-2-fluorobenzoyl)-4-methoxyS-(1-methylethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

RN 348167-00-0 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono-4-[2-(3-chloro-2-fluorobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

CH2-CO2H

348167-11-3 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-(5-(2-cyclopentylethyl)-4-methoxy-2-(3-methylbenzoyl)phenoxyl- (9CI) (CA INDEX NAME)

348167-14-6 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-{5-iodo-4-methoxy-2-(3-methylbenzoyl)phenoxy}-, methyl ester (9CI) (CA INDEX NAME)

6/23/2003

ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
348167-15-7 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-(5-iodo-4-methoxy-2-(3-methylbenzoyl)phenoxy)- (9C1) (CA INDEX NAME)

348167-20-4 CAPLUS
Benzeneacetic acid, 4-[5-(acetylamino)-4-methoxy-2-(3-methylbenzoyl)phenoxyl-3,5-dibromo-, methyl ester (9CI) (CA INDEX NAME)

348167-21-5 CAPLUS

Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-(3-methylbenzoyl)-5-[(3-methylbenzoyl)amino]phenoxyl-, methyl ester (9CI) (CA INDEX RAME)

ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
348167-27-1 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-hydroxy-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

348167-28-2 CAPLUS Benzeneacetic acid, dibromo-4-[2-(3-methylbenzoyl)-5-(1-methylethyl)-4-(2-methylpropoxy)phenoxy)- (9CI) (CA INDEX NAME)

i-BuC

IT 348166-63-8P 348166-51-8P 348166-59-6P
348166-22-1P 348166-82-5P 348166-93-8P
348166-93-3P
RI: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or respent); USS (Uses)
(prepn. of di-Ph ether liver selective glucocorticoid receptor antagonists starting from phenols and diphenyliodonium salts)
RN 348166-43-8 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-(2-[hydroxy(2-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy)- (9CI) (CA INDEX NAME)

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L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

348167-22-6 CAPLUS
Benzeneacetic acid, 4-[5-(acetylamino)-4-methoxy-2-(3-methylbenzoyl)phenoxy]-3,5-dibromo- (9CI) (CA INDEX NAME)

348167-25-9 CAPLUS Bearage acid, 3,5-dibromo-4-[4-hydroxy-2-(3-methylbenzoyl)-5-(1-methylthyl)phenoxyl- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

348166-51-8 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-[methoxy(3-methylphenyi]methyl]n-5-[1-methylethyl]phenoxy]- (9CI) (CA INDEX NAME)

348166-59-6 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-[(3-methylphenyl)(4-nitrophenoxy)methyl]phenoxy]- (9CI) (CA INDEX NAME)

348166-62-1 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-[chloro(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy)- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OP 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

348166-82-5 CAPLUS
Benzeneacetic acid, 3.5-dibromo-4-[2-[hydroxy(4-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 348166-93-8 CAPLUS
CN Benzeneacetic acid,
3,5-dibromo-4-[2-[(3,5-dimethylphenyl)hydroxymethyl]-4methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

348166-98-3 CAPLUS
Benzeneactic acid, 3,5-dibromo-4-[2-{[3-chloro-2-fluorophenyl]hydroxymethyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI)
(CA INDEX NAME)

ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

348166-41-6 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-[[2-(methylsulfonyl)ethoxy]phenylmethyl]phenoxy]- (9CI) (CA INDEX NAME)

348166-44-9 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-{2-{(2,4-difluorophenoxy){2-methylphenyl}methyl}-4-methoxy-5-{1-methylethyl}phenoxy}- (9CI) (CA

348166-48-3 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-(4-methoxy-5-(1-methylethyl)-2-((2-methylphenyl)[(2-methylpropyl)amino]methyl]phenoxy]- (9CI) (CA INDEX NAME)

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ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

348166-50-7 CAPLUS Benzeneacetic acid, 3,5-dibromo-4-[2-[hydroxy(3-methylpheny1]methyl]-4-methoxy-5-(1-methylethyl)phenoxy)- (9CI) (CA INDEX NAME)

348166-53-0 CAPLUS Benzeneacetic acid, 3,5-dibromo-4-(4-methoxy-2-((1-methylethoxy) (3-methylphemyl)methyl)-5-(1-methylethyl)phemoxy)- (9CI) (CA INDEX NAME)

348166-55-2 CAPLUS
Benzeneacetic acid, 3.5-dibromo-4-[2-((cyclohexyloxy)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 348166-57-4 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-{(4-fluorophenoxy)(3-methylphenyl)methyl}-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 348166-58-5 CAPLUS
CN Benzenacetic acid, 3,5-dibromo-4-[4-methoxy-2-[(4-methoxyphenoxy)(3-methylphenyl)methyll-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 348166-63-2 CAPLUS
CN Benzeneacetic acid, 4-[2-[amino(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxyl-3,5-dibromo- (9CI) (CA INDEX NAME)

RN 348166-64-3 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-[[(1-methylethyl)amino](3-methylphenyl)methyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 348166-67-6 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-(2-{(cyclopropylamino)(3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

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L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 348166-60-9 CAPLUS
CN Benzeneacetic acid, 4-{2-[(4-aminophenoxy)(3-methylphenyl)methyl]-4methoxy-5-(1-methylethyl)phenoxy)-3,5-dibromo-(9Cl) (CA IMDEX NAME)

RN 348166-61-0 CAPLUS
CN Benzeneacettc acid, 3,5-dibromo-4-[2-[[(4-hydroxybenzoyl)oxy](3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 348166-68-7 CAPLUS
CN Benzeneactic acid, 3,5-dibromo-4-(4-methoxy-5-(1-methylethyl)-2-[(3-methylphenyl)-1-pyrrolidinylmethyl]phenoxy)- (9CI) (CA INDEX NAME)

RN 148166-69-8 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-[(3-methylphenyl)-1-piperidinylmethyl|phenoxy]- (9CI) (CA INDEX NAME)

RN 348166-70-1 CAPLUS Benzeneacetic acid, 3,5-dibrono-4-14-methoxy-2-[(2-methoxyethyl)amino](3-methylphenyl)methyl]-5-(1-methylethyl)phenoxyl- (9CI) (CA INDEX NAME) 6/23/2003

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

MeO. CH2-CH2-OME

RN 348166-71-2 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[[[2-(diethylamino)ethyl]amino](3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy)- (9CI) (CA

INDEX

MEO CH\_ CH\_ NEt\_

RN 348166-72-3 CAPLUS

Senzeneacetic acid, 3.5-dibromo-4-(4-methoxy-5-(1-methylethyl)-2-[(3-methylphenyl)][[2-(1-piperidinyl)ethyl]amino]methyl]phenoxy]- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 348166-75-6 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[{(3-carboxyphenyl)amino](3-methylphenyl)methyl}-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CAINDEX

RN 348166-76-7 CAPLUS
CN Benzeneacetic acid, 3.5-dibromo-4-[2-[[(4-hydroxybenzoy1)amino](3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX
NAMP)

Habte

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L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 348166-73-4 CAPLUS
CN Benzeneactic acid, 3,5-dibromo-4-[4-methoxy-5-[1-methylethyl)-2-[(3-methylphenyl)-1-piperazinylmethyl]phenoxyl- (9C1) (CA INDEX NAME)

RN 348166-74-5 CAPLUS

Senzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-[[[4-methoxyphenyl]methyl]amino|(3-methylphenyl)methyl]-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 34B166-77-8 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-[(3-methylphenyl)[[(4-methylphenyl)sulfonyl]amino]methyl]phenoxy]- (9CI) (CA INDEX NAME)

RN 348166-78-9 CAPLUS
CN Benzeneactic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylathyl)-2-[(3-methylphenyl)[(jhenylmethyl)thio]methyl]phenoxy)- [9CI) (CA INDEX NAME)

RN 348166-79-0 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-{[(2-furanylmethyl)thio](3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy}- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued

RN 348166-80-3 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[((carboxymethyl)thio](3-methylphenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxyl- (9CI) (CA INDEX NAME)

RN 348166-83-6 CAPLUS Senzeneacetic acid, 3,5-dibromo-4-[4-methy2-2-[(1-methylethoxy) (4-methylpheny)]methyl]-5-(1-methylethyl)phenoxyl (CA INDEX NAME)

RN 348166-84-7 CAPLUS CN Benzeneacetic acid, 3,5-dibromo-4-[2-[hydroxy[3-[1-

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
CN Benzeneacetic acid, 3,5-dibromo-4-[2-{hydroxy}[3(trifluoromethyl)phenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxyl(9CI)

RN 348166-88-1 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-[methoxy[3-(trifluoromethyl)phenyl]methyl]-5-(1-methylethyl)phenoxyl- (9CI) (CA INDEX NAME)

RN 348166-89-2 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-[hydroxy[3-(trifluoromethoxy)phenyl]methyl]-4-methoxy-5-(1-methylethyl)phenoxy](9CI) (CA INDEX NAME)

RN 348166-90-5 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono-4-[2-[3-[dimethylamino]phenyl]hydroxymeth
yl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

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L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
methylethyl)phenyl]methyl]-4-methoxy-5-{1-methylethyl)phenoxy}- (9CI)
(CA
INDEX NAME)

RN 348166-85-8 CAPLUS
CN Benzenescetic acid, 3,5-dibromo-4-[2-{(3-fluorophenyl)hydroxymethyl]-4methoxy-5-[1-methylethyl]phenoxy]- (9C1) (CA INDEX NAME)

RN 348166-86-9 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[hydroxy(3-iodophenyl)methyl]-4-methoxy-5-(1-methylethyl)phenoxy]- [9CI] (CA INDEX NAME)

RN 348166-87-0 CAPLUS

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 348166-96-1 CAPLUS

Benzeneacetic acid, 3,5-dibromo-4-[2-((cyclohexyloxy) (3,5-dimethylphenyl)methyl)-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 348166-97-2 CAPLUS
CN Benzeneacetic acid,
3,5-dibromo-4-[2-[(1,5-difluorophenyl)hydroxymethyl]-4methoxy-5-(1-methylethyl)phenoxy)- (9CI) (CA INDEX NAME)

RN 348167-01-1 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-[(3-chloro-2-fluoropheny)]methoxymethyl]-4-methoxy-5-(1-methylethyl)phenoxy)- (9CI)
6/23/2003

ANSWER 4 OP 6 CAPLUS COPYRIGHT 2003 ACS (Continued) (CA INDEX NAME)

348167-02-2 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-[4-fluoro-3-methylphenyl)hydroxymethyl]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI)
(CA INDEX NAME)

348167-05-5 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[5-(2-cyclopentylethyl)-2-[hydroxy(3-methylphenyl)methyl)-4-methoxyphenoxy]- (9CI) (CA INDEX NAME)

ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

348167-26-0 CAPLUS
Benzeneacetic acid,
-dibromo-4-[2-[hydroxy(3-methylphenyl)methyl]-5-{1methylethyl}-4-(2-methylpropoxy)phenoxy]- (9CI) (CA INDEX NAME)

348167-29-3 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-(2-fluoroethoxy)-2-[hydroxy(3-methylphenyl)methyl)-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

348167-30-6 CAPLUS
Benzenepropanoic acid,
-dibromo-4-[2-(hydroxy(3-methylphenyl)methyl]-4methoxy-5-(1-methylethyl)phenoxy|- (9CI) (CA INDEX NAME)

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ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

348167-12-4 CAPLUS
Benzeneacetic acid, 3.5-dibromo-4-{2-[hydroxy(3-methylphenyl)methyl]-5-iodo-4-methoxyphenoxy]- (9CI) (CA INDEX NAME)

RN 348167-16-8 CAPLUS
CN Benzeneacetic acid,
4-[5-(acetylamino)-2-[hydroxy(3-methylphenyl)methyl]-4methoxyphenoxyl-3,5-dibromo- (9CI) (CA INDEX NAME)

348167-23-7 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-[hydroxy(3-methylphenyl)methyl]-4-methoxy-5-[(3-methylbenzoyl)amino]phenoxy]- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

348166-66-5

34816-66-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of di-Ph ether liver selective glucocorticoid
receptor antagonists starting from phenole and diphenyliodonium selts)
348166-66-5 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-(chloro(3-methylphenyl)methyl)-4methoxy-5-(1-methylethyl)phenoxy)-, methyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 5 OF 6
ACCESSION NUMBER: 2000:117013 CAPLUS
DOCUMENT NUMBER: 132:166010
Freparation of 4-phenoxyphenylacetic acids as glucocorticoid and thyroid hormone receptor ligands for the treatment of metabolic disorders
Apalgyist. Thereas; Goede, Patrick; Holmgren, Erik
AFRON STORES: PIXXD2
DOCUMENT TYPE: Patent LANGUAGE: English
FAMILY ACC. NUM. COUNT: PIXXD2
PATENT INPRIMATION.

PAMILY ACC. NUM. COUNT:

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ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

258819-45-3 CAPLUS
Benzeneacetic acid, 4-(2-benzoyl-4-hydroxy-5-(1-methylethyl)phenoxy]-3,5-dibromo-, methyl ester (9CI) (CA INDEX RAME)

IT 258819-43-1P 258819-47-5P 258819-50-0P
258819-51-1P 258819-53-3P 258819-56-6P
258819-51-1P 258819-53-3P 258819-56-6P
258819-60-4P 258819-61-4P 258819-61-4P
258819-60-4P 258819-61-4P 258819-65-7P
258819-66-4P 258819-67-9P 258819-68-0P
258819-69-1P 258819-67-9P 258819-74-0P
258819-78-3P 258819-73-7P 258819-74-0P
258819-78-3P 258819-73-7P 258819-74-0P
258819-78-3P 258819-79-3P 258819-74-0P
258819-78-3P 258819-79-3P 258819-68-P
258819-81-7P 258819-79-3P 258839-63-9P
258819-91-3P RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-phenoxyphenylacetic acide as glucocorticoid and thyroid
hormone receptor ligands for the treatment of metabolic disorders)
RN 258819-43-1 CAPLUS
Benzeneacetic acid,
3,5-dibromo-4-12-[(4-chlorophenyl)acetyl]-4-methoxy-5(1-methylethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

Page 27

ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

The title compds. [I; R1 = alkyl, aryl, CO2H, etc.; R2, R3 = H, halo, alkyl, etc. (at least one of R2 and R3 being other than hydrogen); X =

CH2; R4 = alkyl, aryl, heteroaryl; R5 = halo, alkyl, cycloalkyl; Y = OH, OMe, NH2, alkylamino; n = 0-4], useful for treating diseases assocd. with metab. dysfunction or which are dependent on the expression of a glucocorticoid or thyroid receptor gene (such as diabetes, hypercholesterolemie, or obesity) (no data), were prepd. E.g., a multi-step synthesis of ester I [R1 = CO2Me; n = 1; R2 = R3 = Br; Y =

OMe;

R4 = Ph; X = CO; R5 = iso-Pr] was given. Compds. I are effective at 0.5-25 mg/kg/day.

IT 252043-41-19 252201-98-2P 258819-45-3P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (prepn. of 4-phenoxyphenylacetic acide as glucocorticoid and thyroid hormone receptor ligands for the treatment of metabolic disorders)

RN 252043-61-1 CAPIUS

CN Benzeneacetic acid, 4-[2-benzoyl-4-methoxy-5-(1-methylethyl)phenoxy]-3,5-dibromo-, methyl ester (9CI) (CA INDEX NAME)

252201-98-2 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-(4-methoxy-2-(3-methylbenzoyl)-5-(1-methylthyl)phenoxyl- (9C1) (CA INDEX NAME)

ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

258819-47-5 CAPLUS Benzeneacetic acid, 4-[2-benzoyl-4-hydroxy-5-(1-methylethyl)phenoxy]-3,5-dibromo-(9CI) (CA INDEX NAME)

258819-50-0 CAPLUS Benzeneacetic acid, 3,5-dibromo-4-[2-[4-(1,1-dimethylethyl)benzoyl]-4-hydroxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

258819-51-1 CAPLUS
Benzeneacetic acid, 4-[2-benzoyl-4-methoxy-5-(1-methylethyl)phenoxy]-3,5-dibromo-(9c1) (CA INDEX NAME)

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 258819-53-3 CAPLUS
CN Benzeneacetic acid, 4-[4-methoxy-5-(1-methylethyl)-2(phenylmethyl)phenoxy|- (9CI) (CA INDEX NAME)

RN 258819-56-6 CAPLUS
CN Benzeneacetic acid. 3,5-dibromo-4-[2-(2-fluorobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 258819-57-7 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-(3-fluorobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 258819-61-3 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-(diphenylacetyl)-4-methoxy-5-(1-methylethyl)phenoxy)- (9CI) (CA INDEX NAME)

RN 258819-62-4 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-{2-(3-chlorobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 258819-63-5 CAPLUS
CN Benzenezetic ecid, 3,5-dibromo-4-(2-(4-chlorobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxyl- (9C1) (CA INDEX NAME)

### Page 28

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 258819-58-8 CAPLUS

Senzeneacetic acid, 3,5-dibromo-4-[2-(4-fluorobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxy]- (3CI) (CA INDEX NAME)

RN 258819-59-9 CAPLUS CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-(2-methylbenzoyl)-5-(1-methylethyl)phenoxy)- (9CI) (CA INDEX NAME)

RN 258819-60-2 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-(4-methylbenzoyl)-5-(1-methylethyl)phenoxy)- (9C1) (CA INDEX NAME)

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 258819-64-6 CAPLUS
CN Benzenacetic acid, 3,5-dibromo-4-[2-(3-bromobenzoy1)-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 258819-65-7 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-(2-(3-iodobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxyl- (9CI) (CA INDEX NAME)

RN 258819-66-8 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[2-(4-iodobenzoyl)-4-methoxy-5-(1-meth)ylethyl)phenoxy)- (SCI) (CA INDEX NAME)

#### L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 358819-67-9 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-(3-nitrobenzoyl)phenoxy)- [9CI] (CA INDEX NAME)

RN 258819-68-0 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-[3-(trifluoromethyl)benzoyl]phenoxy]- [9C1] (CA INDEX NAME)

RN 258819-69-1 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-(2-(3-hydroxybenzoy1)-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

### L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued methylphenyl)methyl]phenoxy] - (9CI) (CA INDEX NAME)

RN 258819-76-0 CAPLUS
CN Benzeneacetic acid,
3,5-dibromo-4-{2-{13-iodophenyl}methyl}-4-methoxy-5-{1-methylethyl}phenoxy]- (9CI) (CA INDEX NAME)

258819-77-1 CAPLUS
CN Benzenepropanoic acid, 3,5-dibromo-4-[4-methoxy-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 258819-78-2 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-{4-methoxy-5-(1-methylethyl)-2-[3-(phenylethynyl)benzoyl]phenoxy)- (9CI) (CA INDEX NAME)

### Habte

### Page 29

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 258819-73-7 CAPLUS

Senzeneacetic acid, 4-[2-[3,5-bis(1,1-dimethylethyl)benzoyl}-4-methoxy-5(1-methylethyl)benzoyl-3,5-dibromo- (9CI) (CA INDEX NAME)

RN 258819-74-8 CAPLUS
CN Benzeneacetic acid,
3,5-discomo-4-[2-(3,5-discompany)]-4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 258819-75-9 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-[(3-

### L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 258819-79-3 CAPLUS
CN Benzeneacetic acid,
3,5-dibromo-4-[2-[3-[(3-hydroxyphenyl)ethynyl]benzoyl]4-methoxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

RN 258819-80-6 CAPLUS
CN Benzeneacetic acid, 3,5-dibromo-4-(2-(3-ethynylbenzoyl)-4-methoxy-5-(1-methylethyl)phenoxyl-(9CI) (CA INDEX NAME)

RN 258819-81-7 CAPLUS

Senzeneacetic acid, 3,5-dibromo-4-[2-{3-(3-hydroxy-1-propynyl)benzoyl}-4-methoxy-5-(1-methylethyl)phenoxyl- (9CI) (CA INDEX NAME)

### 6/23/2003

ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 258819-82-8 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono-4-[4-methoxy-5-[1-methylethyl]-2-[3-(3-oxo-1-pentenyl]benzoyl]phenoxy]- (9CI) (CA INDEX NAME)

258819-83-9 CAPLUS
Benzeneacetamide, 3,5-dibromo-4-{4-methoxy-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxy}- (9CI) (CA INDEX NAME)

258819-91-9 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-hydroxy-5-(1-methylethyl)-2-(phenylmethyl)phenoxy)- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

258819-95-3 CAPLUS
Benzeneacetic scid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl),-2-(phenylmethyl)phenoxy|-, methyl ester (SCI) (CA INDEX NAME)

258819-96-4 CAPLUS
Benzeneacetic acid, 4-[4-methoxy-5-(1-methylethyl)-2(phenylmethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAMS)

258819-99-7 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-(2-(2-fluorobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxyl-, methyl ester (9CI) (CA INDEX NAME)

### Page 30

ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS

252043-62-2P 258819-94-2P 258819-95-3P
258819-96-4P 258819-99-7P 258820-00-7P
258820-01-8P 258820-03-5P 258820-04-3P
258820-04-1P 258820-05-3P 258820-06-3P
258820-07-4P 258820-11-0P 258820-12-1P
258820-10-9P 358820-11-0P 258820-12-1P
258820-19-8P 258820-20-1P 258820-12-1P
258820-22-3P 258820-20-1P 258820-21-2P
258820-22-3P 258820-21-4P 258820-24-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); (prepn. of 4-phenoxyphenylacetic acids as glucocorticoid and thyroid hormone receptor ligands for the treatment of metabolic disorders)
252043-62-2 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-(3-methylbenzoy1)-5-(1-

Paraenacetic acid, 3,5-dibromo-4-[4-methoxy-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxy)-, methyl ester (9CI) (CA INDEX NAME)

258819-94-2 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-[4-(1,1-dimethylethyl)benzoyl]-4-hydroxy-5-(1-methylethyl)phenoxy)-, methyl ester (9CI) (CA INDEX RAME)

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

258820-00-7 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-(2-(3-fluorobenzoy1)-4-methoxy-5-(1-methylethyl)phenoxyl-, methyl ester (9CI) (CA INDEX NAME)

258820-01-8 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-(2-(4-fluorobenzoyl)-4-methoxy-5-(1-methylathyl)phenoxyl-, methyl ester (9CI) (CA INDEX NAME)

258B20-02-9 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-{4-methoxy-2-(2-methylbenzoyl)-5-{1-methylthyllphenoxyl-, methyl ester (9CI) (CA INDEX NAME)

#### L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

# RN 258820-03-0 CAPLUS CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-(4-methylbenzoyl)-5-(1-methylethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

# RN 258820-04-1 CAPLUS CN Benzeneacetic acid, 3,5-dibromo-4-[2-(diphenylacetyl)-4-methoxy-5-(1-methylethyl)phenoxy)-, methyl ester (9CI) (CA INDEX NAME)

### RN 258820-05-2 CAPLUS CN Benzeneacetic acid, 3,5-dibromo-4-[2-(3-chlorobenzpyl)-4-methoxy-5-(1-methylethyl)phenoxyl-, methyl ester (9CI) (CA INDEX RAME)

### L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

# RN 258820-09-6 CAPLUS CN Benzeneacetic acid, 3,5-dibromo-4-{2-(4-iodobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxy)-, methyl eater (9CI) (CA INDEX NAME)

# RN 258820-10-9 CAPLUS CN Benzeneacetic acid, 3,5-dibromo-4-{4-methoxy-5-{1-methylethyl}-2-{3-nitrobenzoyl}phenoxyl-, methyl ester (9CI) (CA INDEX.NAME)

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# RN 258820-11-0 CAPLUS CN Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-[1-methylethyl]-2-[3[trifluoromethyl]benzoyl]phenxy]-, methyl ester (9CI) (CA INDEX NAME)

### Page 31

#### L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

### N 258820-06-3 CAPLUS Benzeneacetic acid, 3,5-dibromo-4-(2-(4-chlorobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxyl-, methyl ester (9CI) (CA INDEX NAME)

# RN 258820-07-4 CAPLUS CN Benzeneacetic acid, 3,5-dibromo-4-[2-(3-bromobenzoy1)-4-methoxy-5-(1-methylethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

# .N 258820-08-5 CAPLUS CN Benzeneacetic acid, 3,5-dibromo-4-[2-(3-iodobenzoyl)-4-methoxy-5-(1-methylethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

### L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

### RN 258820-12-1 CAPLUS CN Benzeneacetic acid, 4-[2-[3-(acetyloxy)benzoyl]-4-methoxy-5-(1methylethyl)phenoxyl-3,5-dibromo-, methyl ester (9CI) (CA INDEX NAME)

# RN 258820-16-5 CAPLUS CN Benzeneacetic acid, 4-[2-[3,5-bis(1,1-dimethylethyl)benzoyl]-4-methoxy-5(1-methylethyl)phenoxy]-3,5-dibromo-, methyl ester (9CI) (CA INDEX NAME)

# RN 258820-17-6 CAPLUS CN Benzeneacetic acid, 3,5-dibrono-4-[2-(3,5-difluorobenzoyl)-4-methoxy-5-(1methylethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

258820-18-7 CAPLUS
BENZENEACETIC acid,
-dibromo-4-[2-[(3-iodophenyl)methyl]-4-methoxy-5-(1methylethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

258820-19-8 CAPLUS
Benzenepropanoic acid, 3,5-dibromo-4-[4-methoxy-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

258820-23-4 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[2-[3-(3-hydroxy-1-propynyl)benzoyl]-4methoxy-5-(1-methylethyl)phenoxyl-, methyl ester (9CI) (CA INDEX NAME)

RN 258820-24-5 CAPLUS
CN Benzeneacetic acid,
3,5-dibrono-4-[4-methoxy-5-(1-methylethyl)-2-[3-(3-oxo1-pentenyl)benzoyl]phenoxyl-, methyl ester (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

### Page 32

ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS

258820-20-1 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-[3-(phenylethynyl)benzoyl]phenoxyl-, methyl ester (9CI) (CA INDEX NAME)

258820-21-2 CAPLUS

RN 25830-2-2 Graud

CR Benzeneacetic acid,

3,5-dibromo-4-[2-[3-[(3-hydroxyphenyl)ethynyl]benzoyl]4-methoxy-5-(1-methylethyl)phenoxyl-, methyl ester (9CI) (CA INDEX NAME)

258820-22-3 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-5-(1-methylethyl)-2-[3-[(trimethylsilyl)ethynyl]benzoyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER:
DOCUMENT NUMBER:
11999:795614 CAPLUS
132:30840
KB 285 in treatment of diabetes
KB 285 in treatment of diabetes
Apelqvist, Thereas, Etendic, Suad
Karo Bio AB, Swed.
SOURCE:
CODEN: PIXXD2
DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
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A liver-selective glucocorticoid antagonist, preferably KB285 (I) is prepd. and used in the prepn. of a pharmaceutical compns. for the treatment of diabetes. In adda. to synthetic examples, receptor binding 6/23/2003

L4 ANSMER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
and cell based assays are given.

IT 32301-98-2P, KB 285
R1: BAC (Biological activity or effector, except adverse); BSU (Biological actudy, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)

(KB 285 in treatment of diabetes)
RN 325201-98-2 CAPLUS
CN Benzenescetic acid, 3,5-dibromo-4-[4-methoxy-2-(3-methylbenzoyl)-5-[1-mathylethyl]phenoxy]- (9CI) (CA INDEX NAME)

252043-61-1P 252043-62-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(KB 285 in treatment of diabetes)
252043-61-1 CAPLUS
Benzenecetic acid, 4-[2-benzoyl-4-methoxy-5-(1-methylethyl)phenoxy]-3,5-dibromo-, methyl ester (9CI) (CA INDEX NAME)

252043-62-2 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-2-(3-methylbenzoyl)-5-(1-methylethyl)phenoxyl-, methyl ester (9CI) (CA INDEX NAME)

ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS

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=> log y COST IN U.S. DOLLARS SINCE FILE TOTAL SESSION ENTRY 176.39 27.63<sup>-</sup> FULL ESTIMATED COST SINCE FILE TOTAL DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) ENTRY SESSION -3.91 -3.91 CA SUBSCRIBER PRICE

STN INTERNATIONAL LOGOFF AT 15:57:05 ON 25 JUN 2003

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STR

G1 O, S, N, CH2, CH, CF2, SO2, NH

G2 0, S

G3 O, N

G4 C, S, N, CH, CF2, Ak

G5 H, Et, n-Pr, i-Pr, n-Bu, i-Bu, s-Bu, t-Bu, Me

G6

G7 H, CN, X, Cb, Ak, CH2, CH, CF2, CF3

G8 H, Ak

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 15:32:52 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 18163 TO ITERATE

5.5% PROCESSED

1000 ITERATIONS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

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FULL FILE PROJECTIONS:

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6/23/2003

Page 4

10/082,022

SEARCH TIME: 00.00.10

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78 SEA SSS FUL L1

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COST IN U.S. DOLLARS

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SESSION

FULL ESTIMATED COST

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FILE COVERS 1907 - 25 Jun 2003 VOL 138 ISS 26 FILE LAST UPDATED: 24 Jun 2003 (20030624/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L4 ANSMER 1 OF 20 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:173554 CAPLUS
DOCUMENT NUMBER: 138:221353
Preparation of aryloxyphenols as thyroid receptor antagonists for the treatment of cardiac and

INVENTOR (S) Koehler,

disorders Malm, Johan; Brandt, Peter; Edvinsson, Karin;

Konrad; Sanin, Andrei; Gordon, Sandra Karo Bio AB, Swed. PCT Int. Appl., 42 pp. CODEN: PIXXD2 Patent English 1

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

KIND DATE PATENT NO. APPLICATION NO. DATE 20020813 20020813 BZ, CA, GB, GD, KZ, LC, NO, NZ, TN, TR, KG, KZ, AT, LU, GW,

A 20010824 A 20020403

OTHER SOURCE(S):

GB 2001-20691 GB 2002-7719 MARPAT 138:221353

ANSWER 1 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued) (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Uses)

(aryloxyphenols as thyroid receptor antagonists for treatment of cardiac and metabolic disorders)
500794-84-3 CAPLUS
Benzenepropanoic acid,
-dibromo-4-(4-hydroxy-1-(1-methylethyl)-5-{(1E)2-phenylethenyl]phenoxy]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

500794-95-6 CAPLUS Benzenepropanoic acid, 3,5-dibromo-4-[3-[(1E)-2-[4-

ethylamino)methyl]phenyl]ethenyl]-4-hydroxy-5-(1-methylethyl)phenoxy]-(9CI) (CA INDEX NAME)

Double bond geometry as shown

RN 500794-97-8 CAPLUS .
CN Benzenepropanoic acid, 3,5-dibrono 4-(3-{(1E}-2-(4-carboxypheny1)-theny1)-4-bydroxy-5-(1-methylethyl)phenoxy]- (9CI) (0

(CA INDEX NAME)

Double bond geometry as shown.

Page 5

ANSWER 1 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

Title compds. I [R1 = carboxy, ester, .alpha.-hydroxycarboxy, etc.; R2-3

Cl, I, Br, alkyl, haloalkyl, alkenyl, etc.; R4 = halo, alkyl, alkenyl, alkynyl, etc.; X = CH2CH2, CH2CH2CH2, CH-CH, etc.; R5 = (hetero)aryl, cycloalkyl, etc.; n = 0-2) are prepd. For instance, Me 3,5-dibromo-4-(3-isopropyl-4-methoxyphenoxy)benzoate is nitrated (PhH, HNO3), reduced (EtOH, Na28204) and converted to Me -dibromo-4-(3-isopropyl-4-methoxyphenoxy)benzoate (MeOH, HCl, KI). This intermediate was aspond. (EtOH, KOH), demethylated (CH2Cl2, BF3.bul.SMe2) and coupled to styrene (DMF, Et3N, Me3NCH2PhCl, sidibenzylideneacetone)dipalladium) to give II. The compds. of the invention exhibit binding affinities to the ThR.alpha. receptor in the range of 10 to 500 nM. I are useful in

treatment of cardiac and metabolic disorders, such as cardiac

/thmias,
thmias,
thyrotoxicosis, subclin. hyperthyroidism and liver diseases.
500794-84-1P 500794-95-6P, (E) -3-{3,5-Dibromo-4-{3-{2-(4((dimethylamino)methyl)phenyl)} ethenyl] -4- hydroxy-5isopropylphenoxylphenyllpropionic acid 500794-97-8P,
(E) -4-{2-{5-{2,6-Dibromo-4-{2-carboxyethyl)phenoxyl-2-hydroxy-3isopropylphenyl]ethenyl]benzoic acid 500795-00-6P,

3-(3,5-Dibromo-4-(4-hydroxy-3-isopropyl-5-(phenethyl)phenoxy)phenyl|propio nic acid 500795-02-8P, (E)-3-(3,5-Dibromo-4-(4-hydroxy-3-isopropyl-5-(2-phenylethenyl)phenoxy)phenyl|-2-hydroxypropionic acid 500795-11-9P, 3-(3,5-Dibromo-4-(4-hydroxy-3-isopropyl-5-(phenethyl)phenoxy)phenyl|-2-hydroxypropionic acid RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

ANSWER 1 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

500795-00-6 CAPLUS Benzenepropanoic acid, 3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)-5-(2-phenylethyl)phenoxy)- (9CI) (CA INDEX NAME)

500795-02-8 CAPLUS

Benzenepropanoic acid, 3,5-dibromo-.alpha.-hydroxy-4-[4-hydroxy-3-(1-methylethyl)-5-[(1E)-2-phenylethenyl]phenoxy]- (9CI) (CA INDEX NAME)

Double bond geometry as

500795-11-9 CAPLUS
Benzenepropanoic acid, 3,5-dibromo-.elpha.-hydroxy-4-[4-hydroxy-3-(1-methylethyl)-5-(2-phenylethyl)phenoxy]- (9CI) (CA INDEX NAME)

6/23/2003

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L4 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

TS 500795-01-7P, Methyl (E)-3-[3,5-dibromo-4-[4-hydroxy-3-isopropyl-5-(2-phenylethenyl)phenoxy]phenyl]propionate 500795-08-4P, Methyl (E)-3-[3,5-dibromo-4-[4-hydroxy-3-isopropyl-5-(2-phenylethenyl)phenoxy]phenyl]-2-hydroxypropionate 500795-12-0P, Methyl 3-[3,5-dibromo-4-(4-hydroxy-3-isopropyl-5-(phenethyl)phenoxy)phenyl]-2-hydroxypropionate Ri. RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or resgent) (aryloxyphenole as thyroid receptor antagonists for treatment of cardiac and metabolic disorders)
RN 500795-01-7 CAPLUS
CN Benzenepropanoic acid.
3,5-dibromo-4-(4-hydroxy-3-(1-methylethyl)-5-[(1E)-2-phenylethenyl]phenoxy]-, methyl cater (SCI) (CA INDEX NAME)

Double bond geometry as shown.

Benzenepropanoic acid, 3,5-dibromo-.alpha.-hydroxy-4-{4-hydroxy-3-{1-methylethyl)-5-[(1E)-2-phenylethenyl]phenoxy}-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

Benzenepropanoic acid, 3,5-dibromo-.alpha.-hydroxy-4-[4-hydroxy-3-(1-methylethyl)-5-(2-phenylethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME) 500795-12-0 CAPLUS

L4 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:721656 CAPLUS
DOCUMENT NUMBER: 138:280956
TITLE: A thyroid hormone antagonist that inhibits thyroid hormone action in vivo
AUTHOR(S): Lim, Wayland; Nguyen, Ngoc-Ha; Yang, Ha Yung;

AUTHOR(S): Scanlan,

Scanlan,

Thomas S.; Furlow, J. David

CORPORATE SOURCE:
Sect. Neurobiol., Physiol, Behavior, University of California, Davis, CA, 95616-8519, USA

SOURCE:
Journal of Biological Chemistry (2002), 277(38), 35664-35670

COODEN, JBCHA3; ISSN: 0021-9258

PUBLISHER:
American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE:
Journal
LANGUAGE:
Beglish
Be wheve characterized the newly developed thyroid hormone antagonist NH-3 in both cell culture and in vivo model systems. NH-3 binds Xenopus laevis

thyroid hormone receptors directly in vitro and induces a conformation distinct from agonist-bound receptors. Transcriptional activation of a thyroid hormone response element-condy, reporter gene is strongly inhibited by NN+3 in a dose-dependent manner. In addn., NN+3 prevents X. laevis thyroid hormone receptors from binding to the p160 family of co-activators GRIP-1 and SNC-1 in a two-hybrid assay. To assess the potency of the compd. in vivo, we used induced and spontaneous X. laevis tadpole metamorphosis, a thyroid hormone-dependent developmental process. NN-3 inhibits thyroid hormone-induced morphol. changes in a -dependent

dependent manner and inhibits the up-regulation of endogenous thyroid hormone-responsive genes. Spontaneous metamorphosis is efficiently and reversibly arrested by NH-3 with at least the same effectiveness as the thyroid hormone synthesis inhibitor methimazole. Therefore, NH-3 is the first thyroid hormone antagonist to demonstrate potent inhibition of thyroid hormone action in both cell culture- and whole animal-based assave.

assays. 447415-26-1 RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study) (Chyroid hormone antagonist that inhibits thyroid hormone action in

vivo)
447415-26-1 CAPLUS
Acetic acid, [4-[[4-hydroxy-3-(1-methylethyl)-5-[[4-nitrophenyl]ethynyl]phenyl]methyl]-3,5-dimethylphenoxy]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 34 CITED REFERENCES AVAILABLE FOR

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Page 6

ANSWER 1 OF 20 CAPLUS COPYRIGHT 2003 ACS

L4 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSMER 3 OF 20 CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2002:716241 CAPLUS
DOCUMENT NUMBER: 137:212450
TITLE: Preparation of biphenyl derivatives as thyroid hormone

analogs
Haning, Helmut; Moltering, Michael; Schmidt, Gunter;
Faeste, Christians Dischoft, Hilmar; Krefschmer,
Axel; Voehringer, Verens; Ellinghaus, Peter
Bayer Aktiengesellschaft, Germany
CT Int. Appl., 95 pp.
CODEN: PIXXD2
Patent
German
1 INVENTOR (S)

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE:

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE 20020227 , BZ, CA, , GB, GD, , KZ, LC, , NO, NZ, , TN, TR, , KG, KZ,

OTHER SOURCE(S):

Title compds. [I: X = O. S. SO2, CH2, CHF, CF2, NR8; R8 = H, alkyl; R1,

- H, alkyl; R3, R4 - H, halo, cyano, alkyl, CF3, CHF2, CH2F, vinyl, cycloalkyl; R5 = H, alkyl, halo; R6 = SR9, S(0)nR10, NR11C(0)R12, CH2, etc.; R9 = alkyl, cycloalkyl, alkenyl, aryl, arylmethyl, etc.; n = 1, 2; R10 = OR15, NR16R17, alkyl, cycloalkyl, etc.; R15 = H, Ph, benzyl, alkyl, etc.; R16, R17 = H, (branched) (substituted) alkyl, etc; R11 = H,

ANSMER 3 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)
Propanoic acid, 2-[4-[[3-[(4-fluorophenyl)sulfonyl]-4hydroxyphenyl]methyl]-3,5-dimethylphenoxy]-2-methyl- (9CI) (CA INDEX
NAME)

459430-99-0P 459431-00-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of hiphenyl derivs. as thyroid hormone analogs)
459430-99-0 CAPLUS
Acetic acid, [4-{[3-{(4-fluorophenyl)sulfonyl}-4(phenylmethoxyl)phenyl)methyl]-3,5-dimethylphenoxyl-, ethyl ester (9CI)
(CA INDEX NAME)

459431-00-6 CAPLUS
Propanoic acid, 2-[4-[3:[(4-fluorophenyl)sulfonyl]-4(phenylmethoxy)phenyl]methyl]-3,5-dimethylphenoxy]-2-methyl-, ethyl ester
(SCI) (CA INDEX RAME)

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# Page 7

ANSWER 3 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued) (branched) (substituted) alkyl, etc.; R12 = (branched) (substituted) alkyl, etc.; R12 = (branched) (substituted) alkyl, etc.; R7 = H, alkyl, alkanoyl; Z = YmwCOR36; Y = O, S; m = O, 1; w = (substituted) alkylene; R36 = OR37, NR3RR39; R37-R39 = H, Ph, benzyl, alkyl, etc.), were prepd. as thyroid hormone analogs (no data). Thus, Et (4-(benzyloxy)-3-[(4-fluorophenyl)sulfonyl)benzyl)-3,5-dimethylphenoxylacetate (prepn. given) in EtOH was hydrogenated in the presence of Pd/activated C for 2 h at room temp. and 1013 mbar to give

presence of Pd/activated C for 2 h at room temp. and 1013 mbar to give
864

Et [4-(3-[(4-fluorophenyl)sulfonyl)-4-hydroxybenzyl)-3.5dimethylphenoxy]scetate which was sapond. with 1 N NoON in StON to give
90% [4-(3-[(4-fluorophenyl)sulfonyl)-4-hydroxybenzyl)-3.5dimethylphenoxy]scetic acid. The compds. I are eap. suitable for use in
any indirections that may be treated with natural thyroid hormones such as
depression or thyroid tumor. The inventive compds. I are preferably used
to treat arteriosclerosis, hypercholesterolemia, dyslipidemia as well as
obesity.

IT 459431-01-79

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of biphenyl derive. as thyroid hormone analogs)
RN 459431-01-7 CAPLUS
Acetic acid,
[4-[(3-[(4-fluorophenyl)sulfonyl]-4-hydroxyphenyl)methyl]-3,5dimethylphenoxy]-, ethyl ester (9CI) (CA INDEX NAME)

459431-02-8P 459431-03-9P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Uses)
{prepn. of biphenyl derivs. as thyroid hormone analogs}
RN 459431-02-8 CAPLUS
CN Acetic acid,
[4-[(3-(4-fluorophenyl)sulfonyl]-4-hydroxyphenyl]methyl]-3,5dimethylphenoxyl- (9CI) (CA INDEX NAME)

459431-03-9 CAPLUS

L4 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 4 OF 30 CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2002:457917 CAPLUS DOCUMENT NUMBER: 137:169293

DOCUMENT NUMBER:

Rational Design and Synthesis of a Novel Thyroid Hormone Antagonist That Blocks Coactivator

Recruitmen AUTHOR(S): Nguyen, Ngoc-Ha; Apriletti, James W.; Lima, Suzana T. Cunha; Webb. Paul: Baxter, John D.; Scanlan, Thomas

Program in Chemistry and Chemical Biology,

CORPORATE SOURCE: Departments of Pharmaceutical Chemistry and Cellular and Molecular

Pharmacology, University of California, San Francisco,

CA, 94143-0446, USA Journal of Medicinal Chemistry (2002), 45(15), 3310-3320 CODEN: JMCMAR; ISSN: 0022-2623 American Chemical Society Journal English CASREACT 137:169293 SOURCE:

PUBLISHER: DOCUMENT TYPE: LANGUAGE: OTHER SOURCE(S): GI

The authors report the design and synthesis of a novel series of phenylethynyl derive. I [R = M, (CM2)4Me, NO2, NM2] sharing the halogen-free thyronine scaffold of GC-1 [II). I (R = NO2) is a T3 antagonist with negligible TR agonist activity and improved TR binding affinity and potency that allow for further characterization of its obsd. activity. Its ability to block TR-coactivator interactions appears to be the mechanism for antagonism. It will be a useful pharmacol. tool for further study of T3 signaling and TR function.
447415-19-29 447415-22-79 447415-26-19
447415-19-49
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);

ANSWER 4 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued) methylethyl)phenyl]methyl]-3,5-dimethylphenoxyl- (9CI) (CA INDEX NAME)

446312-33-0P 446312-34-1P 446312-36-3P 446312-37-4P 446312-38-5P 446312-39-6P 446312-40-9P IT

44512-40-79
RE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of phenylethymyl derivs. of GC-1 as thyroid hormone analogs

their binding activity towards thyroid hormone receptors)
446312-33-0 CAPLUS
Acetic acid, [4-[[4-{methoxymethoxy}-3-{1-methylethyl}-5-(phenylethyyl)]henyl]] methyl]-3,5-dimethylphenoxy]-, 1,1-dimethylethyl
ester (9CI) (CA INDEX NAME)

446312-34-1 CAPLUS
Acetic acid, (4-[(4-(methoxymethoxy)-3-(1-methylethyl)-5-[(4-pentylphenyl)ethynyl)phenyl]methyll-3,5-dimethylphenoxyl-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

446312-36-3 CAPLUS Acetic acid, (4-[(4-hydroxy-3-(1-methylethyl)-5-[(4-pentylphenyl)ethynyl]phenyl]methyl]-3,5-dimethylphenoxy}-,1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

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### Page 8

ANSWER 4 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)
BIOL (Biological study); PREP (Preparation)
(prepn. of phenylethynyl derivs. of GC-1 as thyroid hormone analogs

their binding activity towards thyroid hormone receptors)
447415-19-2 CAPLUS
Acetic acid, [4-[(4-hydroxy-3-(1-methylethyl)-5(phenylethynyl)phenyl]methyl]-3,5-dimethylphenoxy]- (9CI) (CA INDEX NAME)

447415-22-7 CAPLUS
Acetic acid, [4-[[4-hydroxy-3-(1-methylethyl)-5-[(4-pentylphenyl)ethynyl]phenyl]methyl)-3,5-dimethylphenoxy)- (9CI) (CA INDEX NAME)

447415-26-1 CAPLUS
Acetic acid, [4-[(4-hydroxy-3-(1-methylethyl)-5-[(4-nttrophenyl)ethynyl]phenyl]methyl]-3.5-dimethylphenoxyl- (9CI) (CA INDEX

447415-29-4 CAPLUS . Acetic acid, [4-[(3-[(4-aminophenyl)ethynyl]-4-hydroxy-5-(1-

ANSWER 4 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

446312-37-4 CAPLUS Acetic acid, [4-[3-[(4-aminophenyl)ethynyl]-4-(methoxymethoxy)-5-(1-methylethyl)phenyl]methyl]-3,5-dimethylphenoxy]-, methyl ester (9CI) (CA INDEX NAME)

446312-38-5 CAPLUS
Acetic acid, [4-[4-(methoxymethoxy)-3-(1-methylethyl)-5-[4nitrophenyl)ethynyl]phenyl]methyl]-3,5-dimethylphenoxy]-, methyl ester
(SCI) (CA INDEX NAME)

$$\bigcap_{\mathsf{MeO-C-CH_2-OMe}}^{\mathsf{Me}} \bigcap_{\mathsf{CH_2-OMe}}^{\mathsf{NO_2}} \bigcap_{\mathsf{CH_2-OMe}}^{\mathsf{NO_2}}$$

446312-39-6 CAPLUS Acetic acid, [4-[(4-hydroxy-3-(1-methylethyl)-5-[(4-nitrophenyl)ethyyl]phenyl]methyl]-3,5-dimethylphenoxy]-; methyl ester (9CI) (CA INDEX NAME)

(Continued) ANSWER 4 OF 20 CAPLUS COPYRIGHT 2003 ACS

$$\begin{array}{c} \text{Me} \\ \text{O} \\ \text{MeO} - \text{C-} \text{CH}_2 - \text{O} \\ \end{array}$$

446312-40-9. CAPLUS
Acetic acid, [4-[[3-[(4-aminophenyl)ethynyl]-4-hydroxy-5-(1-methylethyl)phenyl]methyl)-3,5-dimethylphenoxyl-, methyl ester (9CI) (CAINDEX NAME)

REFERENCE COUNT:

THERE ARE 36 CITED REFERENCES AVAILABLE FOR 36

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 5 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

$$\begin{array}{c} \mathbb{R}^4 \\ \times \\ \times \\ \times \\ \mathbb{R}^3 \end{array} \qquad \begin{array}{c} \mathbb{R}^2 \\ \mathbb{C} \mathbb{H}_2 \Big|_{\mathbb{R}} \mathbb{R}^1 \end{array}$$

The title compds. (I; R1 = alkyl, aryl, CO2H, etc.; R2, R3 = H, halo, alkyl, etc. (at least one of R2 and R3 being other than hydrogen); X =

CH2; R4 = alkyl, aryl, heteroaryl; R5 = halo, alkyl, cycloalkyl; Y = OH, OMe. NH2, alkylamino; n = 0-4], useful for treating diseases assocd. with metab. dyefunction or which are dependent on the expression of a glucocorticoid or thyroid receptor gene (such as diabetes, hypercholestrolemia, or obesity) (no data), were prepd. E.g., a multi-step synthesis of ester I [R1 = CO2Me; n = 1; R2 = R3 = Br; Y =

OMe:

R4 = Ph; X = CO; R5 = iso-Pr] was given. Compds. I are effective at
0.5-25 mg/kg/day.

IT 358819-48-69
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological

logical study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of 4-phenoxyphenylacetic acids as glucocorticoid and thyroid hormone receptor ligands for the treatment of metabolic disorders) 258819-48-6 CAPLUS Benzeneacetic acid, 3.5-dibromo-4-[4-hydroxy-3-(1-methylethyl)-5-(phenylmethyl)phenoxy)- (9CI) (CA INDEX NAME)

сн<sub>2</sub>-- со<sub>2</sub>н

258820-36-9

258820-36-9

(prepn. of 4-phenoxyphenylacetic acids as glucocorticoid and thyroid hormone receptor ligands for the treatment of metabolic disorders)
258820-36-9

CAPLUS
Benzenescetic acid, 3,5-dibromo-4-[4-methoxy-3-(1-methylethyl)-5(phenylmethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

### Page 9

L4 ANSWER 5 OP 20
ACCESSION NUMBER:
DOCUMENT NUMBER:
132:166010
Preparation of 4-phenoxyphenylacetic acids as glucocorticoid and thyroid hormone receptor ligands for the treatment of metabolic disorders
Apelqvist, Theresa; Goede, Patrick; Holmgren, Erik Karo Bio AB, Swed.
SOURCE:
DOCUMENT TYPE:

CAPLUS COPYRIGHT 2003 ACS
2000:117013 CAPLUS
PRICE
132:166010
Preparation of 4-phenoxyphenylacetic acids as glucocorticoid and thyroid hormone receptor ligands for the treatment of metabolic disorders
Apelqvist, Theresa; Goede, Patrick; Holmgren, Erik
Expo Bio AB, Swed.
CODEN: PIXXD2
PATRICE
PRICE
PRICE
2000:117013 CAPLUS
PRICE
132:166010
Preparation of 4-phenoxyphenylacetic acids as glucocorticoid and thyroid hormone receptor ligands for the treatment of metabolic disorders
Apelqvist, Theresa; Goede, Patrick; Holmgren, Erik
PRICE
PRICE
PRICE
PRICE
2000:117013 CAPLUS
2000:117013 CAPLUS
2000:117013 CAPLUS
2000:117013 CAPLUS
2000:117013 CAPLUS
2000:117013 CAPLUS
2010:117013 CAPL DOCUMENT TYPE: Patent English . FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:			
PATENT NO.	KIND DATE	APPLICATION NO. DATE	
WO 2000007972	A1 20000217	WO 1999-IB1447 1999080	34
W: AE, AL,	AM, AT, AU, AZ, BA,	BB, BG, BR, BY, CA, CH, CT	, CU, CZ,
DE. DK.	EE. ES. PI. GB. GD.	GE, GH, GM, HR, HU, ID, II	, IN, IS,
JP. KE.	KG. KP. KR. KZ. LC.	LK, LR, LS, LT, LU, LV, MI	, MG, MK,
		RO, RU, SD, SE, SG, SI, SI	
		VN, YU, ZA, ZW, AM, AZ, BY	
	TJ. TM	.,	
		SZ, UG, ZW, AT, BE, CH, CT	, DE, DK,
		LU. MC. NL. PT. SE. BF. B.	
CI. CM.	GA. GN. GW. ML. MR.	NE. SN. TD. TG	
		CA 1999-2339194 1999080	14
AU 9951881	A1 20000228	AU 1999-51881 1999080	4
AII 753376	B2 20021017		
BR 9912742	A 20010502	BR 1999-12742 199908	04
EP 1102739	A1 20010530	EP 1999-936913 199908	04
EP 1102739	B1 20030423		
		GB, GR, IT, LI, LU, NL, SI	. MC. PT.
	LT. LV. FI. RO	00, 00, 11, 21, 20, 02, 0	
CT 20579	C 20011231	SI 1999-20064 199908	34
JP 2002522407	T2 20020723	JP 2000-563607 1999080	04
AT 238267	E 20030515	JP 2000-563607 199908 AT 1999-936913 199908 BG 2001-105214 200102	04
BG 105214	A 20011231	BG 2001-105214 200102	02
NO 2001000610	A 20010404	NO 2001-610 200102	15
115 6403434	B1 20021210		
PRICEITY APPLA INFO	2. *	US 2001-744865 2001049 3B 1998-16935 A 1998089	05
PRIORITY APPLN. INFO		NO 1999-IB1447 W 199908	
	MARPAT 132:1660		
GI	132.1000		
••			

ANSWER 5 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE 2

FORMAT

L4 ANSWER 6 OP 20 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:623766 CAPLUS
DOCUMENT NUMBER: 125:261263
Positive-working resists containing
t-butoxycarbonylmethyloxybenzene dissolution

inhibitor

for suppressed alkaline impurity Watanabe, Atsushi; Ishihara, Toshinobu; Yagihashi, Fujio; Tanaka, Haruyori; Kawai, Yoshio; Nakamura, INVENTOR (5):

Jiro PATENT ASSIGNEE(S):

Shinetsu Chem Ind Co, Japan; Nippon Telegraph & Teleghone
Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAP
Patent
Japanese 1

DOCUMENT TYPE:

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

KIND DATE APPLICATION NO. JP 08194313
PRIORITY APPLN. INFO.:
OTHER SOURCE(S):
GI A2 JP 1995-20958 1995-20958 19960730 19950113 MARPAT 125:261263

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

TRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

The pos. resists comprise 3 components of an acid generator, a polymer compd., and a dissoln. inhibitor selected from 1.4-bis (bis (4-t-butoxycarbonylmethyloxyphenyl)methyl)enzene, its deriv. I (R1-2 = alkyl; k = 0-4; l = 0-2, k + 1. ltoreq.4), l.3-bis (4-t-butoxycarbonylmethyloxyphenylmethyl)-4, 6-bis-t-butoxycarbonylmethyloxyphenylmethyloxy-2.5-dimethylphenylmethyl-4-t-butoxycarbonylmethyloxyphenzene, its deriv. II (R = N, alkyl), bis (4-t-butoxycarbonylmethyloxyphenzene, its deriv. III (R = alkyl; m = 0-4), 2,2-bis (2,4-di-t-butoxycarbonylmethyloxyphenylphenylmethyl-1-t-butoxycarbonylmethyloxy-4-methylbenzene, and its deriv. V (R = alkyl; m = 0-4), 2,2-bis (2,4-di-t-butoxycarbonylmethyloxy-4-methylbenzene, and its deriv. V (R = alkyl; n=0,1) m = 0-(4-n)). The dissoln. inhibitor suppresses penetration of an alk. impurity in the resist film and provides high-resoln. images.

18216-21-3 18226-26-8 18226-28-5

(pos. resists contg. t-butoxycarbonylmethyloxybenzene dissoln. inhibitor for suppressed alk. impurity)

182216-21-3 CAPLUS

Acetic acid, 2,2'-[(4,6-bis[2-(1,1-dimethylethoxy)-2-oxoethoxy]-1,3-phenylene)bis(methylene-4,1-phenyleneoxy)]bis-, bis(1,1-dimethylethyl)

ester (9CI) (CA INDEX NAME)

L4 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:628058 CAPLUS
DOCUMENT NUMBER: 125:261266
1,3-Bis(4-tert-butoxycerbonylmethyloxyphenylmethyl) - 4,6-bis-tert-butoxycerbonylmethyloxybenzene

for dissolution inhibitor of three-component resist Watenabe, Atsushi; Ishihara, Toshinobu; Yagihashi, Pujio Shinetsu Chem Ind Co, Japan Jpn. Kokai Tokkyo Koho, 4 pp. CODEN: JKXXAF Patent Japansese

INVENTOR(S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

KIND DATE

APPLICATION NO. DATE JP 08193053
PRIORITY APPLN, INFO.:
OTHER SOURCE(S):
GI A2 19960730 JP 1995-20954 JP 1995-20 JP 1995-20954 MARPAT 125:261266

t BuO2CCH2C OCH2CO2t Bu t BuO2CCH2C

The deriv. is I (R = H, alkyl). The deriv. shows good soly, toward macromol. compd. in a three-component pos.-working resist, and is useful for dissoln. inhibitor of the resist.
10216-21-3P 18216-36-8P
RL: PNU (Preparation), unclassified); TEM (Technical or engineered erial use): DRED (Preparation), uses (Uses).

rial
use); PREP (Preparation); USES (Uses)
(prepn. of bis(carbonylmethyloxyphenylmethyl)benzene deriv. for
dissoln. inhibitor of three-component resist)
18215-21-3 CAPLUS
Acetic acid, 2,2'-[14,6-bis[2-{1,1-dimethylethoxy}-2-oxoethoxy]-1,3phenylene|bis(methylene-4,1-phenyleneoxy)|bis-, bis(1,1-dimethylethyl)
ester (9CI) (CA INDEX NAME)

Page 10

ANSWER 6 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 182216-26-8 CAPLUS
CN Acetic acid, 2,2'-[[4,6-bis[2-(1,1-dimethylethoxy)-2-oxoethoxy]-5-methyl1,3-phenylene|bis(methylene-4,1-phenyleneoxy)|bis-,
bis(1,1-dimethylethyl)
ester (9C1) (CA INDEX NAME)

182261-28-5 CAPLUS
Acetic acid, 2,2'-[(4-{2-{1,1-dimethylethoxy}-2-oxoethoxy}-1,3-phenylene|bis|methylene(2,5-dimethyl-4,1-phenylene)oxy}]bis-,
bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

ANSWER 7 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

182216-26-8 CAPLUS
Acetic acid, 2,2'-[[4,6-bis|2-(1,1-dimethylethoxy)-2-oxoethoxy]-5-methyl1,3-phenylene]bis(methylene-4,1-phenyleneoxy)]bis-,
1,1-dimethylethyl)
ester (9CI) (CA INDEX NAME)

Page 11

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L4 ANSWER 8 OF 20
ACCESSION NUMBER:
DOCUMENT MUMBER:
1171LE:
INVENTOR(5):
SOURCE:

DOCUMENT TYPE:
DOCUMENT TYPE:
DOCUMENT TYPE:
DATENT ANSORES:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:

COPPER PEXEM PATENT AND ADDRESSED PUBLISHED PROPRIED PROPRIATION:
EMBRISH PATENT INFORMATION:

COPPER PEXEM PATENT INFORMATION:

1 PATENT INFORMATION:
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DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 691575	A2	19960110	EP 1995-110358	19950703
EP 691575	A3	19960515		
EP 691575	B1	20020320		
R: BE, D	Ε			
JP 08015862	A2	19960119	JP 1994-152218	19940704
JP 3290303	B2	20020610		
JP 08022126	A2	19960123	JP 1994-157278	19940708
JP 3290305	B2	20020610		
JP 08029982	A2	19960202	JP 1994-160143	19940712
JP 3337827	B2	20021028		
US 5824451	A	19981020	US 1995-497795	19950703
PRIORITY APPLN. IN	PO.:		JP 1994-152218 A	19940704
			JP 1994-157278 A	19940708
			JP 1994-160143 A	19940712

A pos. photosensitive compn. comprises (a) a resin sol. in an aq. alkali soln. contg. a specific structure unit, (b) a compd. which generates an acid with irradn. of an active ray or radiation, and (c) a low-mol.-wt. acid-decomposable dissoln. inhibitor having a mol. wt. of not more than 3000, which possesses a tertiary alkyl ester group and whose soly. in an aq. alkali soln. is increased by the action of an acid, wherein compd. (c)

is a compd. having at least two tertiary alkyl ester groups, in which the longest distance with respect to the distance between two tertiary ester groups selected arbitrarily comprises at least 10 bonding atoms except for

the atoms contained in the eater groups or a compd. having at least three tertiary slkyl ester groups, in which the longest distance with respect to

the distance between two tertiary ester groups. The pos. photosensitive compn. has a high sensitivity, high resoln. and good profile and excels ín

storage stability and heat resistance of the resist soln. 173786-59-99

IТ 173786-59-9P
RL: SPN (Synthetic preparation); TEM (Technical or engineered material
use); PREP (Preparation); USES (Uses)
(prepn. and use in pos. photosensitive compns. for lithog. plate
manuf.)
173786-59-9 CAPLUS
Acetic acid, 2,2',2'',2'''-{(1-methylethylidene)bis[{2-{2-(1,1-

dimethylethoxy) -2-oxoethoxy] -5,1,3-benzenetriyl) bis [methylene(2,6-dimethyl-

L4 ANSMER 9 OP 20 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:50352 CAPLUS
DOCUMENT NUMBER: 124:101865
POSITIVE: Yamonaka, Tsukasa; Sakaguchi, Shinji; Kokubo, Tadyoahi; Kawebe, Yasumasa
PATENT ASSIGNEE(S): Fuji Photo Pilm Co Lcd, Japan
SOURCE: CODEN: JKCKAF
DOCUMENT TYPE: Patent
LANGUAGE: PAHLLY ACC. NUM. COUNT: 1

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

KIND DATE DATE APPLICATION NO. JP 07271037 PRIORITY APPLN. INFO.: 19951020 JP 1994-63862 JP 1994-63862 19940331 19940331

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compn. Comprises an alkali sol. resin, a photoacid generator, and gtoreq.1 kinds of compds. selected from I and II (R1-41 - H, XRa1, CN, ODG), X1-10 - single bond, carbonyl, sulfido, sulfonyl, CRblRb2; X single bond, O, S, CO, OGO, NRa1cO, NRa2; Ra1 = C1-10 alkyl, alkyl, alkylene, cycloalkyl, haloalkyl, sryl, alkylaryl, aralkyl; Ra2 = H, Ra1; Rb1, Rb1 + H, Me, Et, C1-4 haloalkyl, De-12 + H, Dinh; Dinh = XIR1; X1 = CRb1Rb2, CRb1Rb2O, CO, CS, COO, COS, CRb1Rb2CO, CRb1Rb2CO, CRb1CR1; CONRb1; Ri = H, C1-20 alkyl, alkenyl, C3-20 cycloalkyl, C6-20 aryl, cumyl, adamantyl, siziRb3ZiRb4ZiRb5, tetrahydro-pyranyl, pyranyl.

1.3-dithia-indane-2-y1;Rb3 - b5 = C1-20 alkyl, cycloalkyl, alkenyl, C6-20 aryl; Zi = single bond, O;

ANSWER 8 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)
4,1-phenylene)oxy}]]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI)
(CA INDEX NAME)

PAGE 1-B

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- oBu-t

ANSWER 9 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 172651-19-3 CAPLUS
CN Acetic sciid,
[2-2-- (methyl-enebis [2-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-5methyl-3,1-phenylenel methylene-4,1-phenyleneoxy]|bis-,
bis(1,1-dimethylethyl)|ester (9C1) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

. о— сн<sub>2</sub>— с— ови- t

L4 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 2-A

RN 172651-22-8 CAPLUS
CN Acetic acid, 2,2'-(methylenebis[[6-[[4-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-2,5-dimethylphenyl]methyl]-4-methyl-2,1-phenylene]oxy]]bis-,bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

PAGE 1-B

RN 172651-25-1 CAPLUS
CN Acetic acid, 2,2'-[[2-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-5-methyl-1,3-phenylene|bis(methylene(6-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-5-methyl-3,1-phenylene|methylene-4,1-phenyleneoxy]|bis-, bis(1,1-dimethylethyl)
ester (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-B

RN 172651-28-4 CAPLUS
CN Acetic acid, 2,2'-[methylenebis[[6-[(4-[2-(1,1-dimethylethoxy)-2-oxoethoxy)]-3-[(4-[2-(1,1-dimethylethoxy)-2-oxoethoxy)] methyl]-achyl]-a-methyl-2,1-phenylenejoxy] bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Page 12

L4 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued

t-Buo-C-CH<sub>2</sub>-0

PAGE -1-B

RN 172651-26-2 CAPLUS
CN Acetic acid, 2.2'-[2-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-5-methyl-1,3phenylene]bis[methylene[6-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-2,5dimethyl-3,1-phenylene]methylene-4,1-phenyleneoxy]|bis-,
bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-A

PAGE 1-B

PAGE 2-A

RN 172651-31-9 CAPLUS
CN Acetic acid, 2,2'-[[2-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-5-methyl-1,3phenylene]bis (methylene)[6-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-2,5dimethyl-3,1-phenylene]methylene[6-[2-(1,1-dimethylethoxy)-2-oxoethoxy]2,5-dimethyl-4,1-phenylene]methylene[2-methyl-4,1-phenylene]oxy]]bis-,
bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-A

PAGE 1-E

172651-32-0 CAPLUS
Acetic acid, 2,2'-[(2,5-dimethyl-1,3-phenylene)bis[methylene[6-[2-(1,1-dimethylethoxy]-2-oxoethoxy]-2,5-dimethyl-3,1-phenylene]methylene[6-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-3,1-phenylene]methylene(2-methyl-4,1-phenylene)oxy]|bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

ANSWER 9 OF 20 CAPLUS COPYRIGHT 2003 ACS

PAGE 1-A

PAGE 1-B

ANSWER 10 OF 20 CAPLUS COPYRIGHT 2003 ACS SSION NUMBER: 1994:450249 CAPLUS MENT NUMBER: 121:50249

ACCESSION NUMBER:

Computer-assisted molecular modeling of

TITLE: benzodiazepine

and thyromimetic inhibitors of the HepG2

iodothyronine AUTHOR (S) :

SOURCE:

membrane transporter Kragie, Laura; Forrester, Maureen L.; Cody, Vivian; McCourt, Mary Fac. Nat. Sci. Math., State Univ. New York, Buffalo, Amberst. NY, 14260, USA Molecular Endocrinology (1994), 8(3), 382-91 CODEN: MCENEN; ISSN: 0888-8809 Journal

CORPORATE SOURCE:

DOCUMENT TYPE: LANGUAGE:

CODEN: MORNEN; ISSN: 0888-8809

MENT TYPE: Journal

IUNGE: English

T3 cellular uptake is inhibited in the presence of benzodiazepines (BZs). The structure-activity relationship of BZ inhibition correlates strongly with halogen substitution of the nonfused Pr ring and indicates that this ring is required for activity. A structure-activity series of thyromimetic (TH) inhibitors of the HepG2 iodothyronine transporter further point out the crit. importance of the amino group of the alanine side chain, its L-stereo configuration, and the size of the substituents of the inner and outer Ph rings. A third series of compds., reported to interact at related sites, were inactive as HepG2 iodothyronine transport inhibitors, and therefore the potent inhibitors were restricted to the BZ and TH compds. Using both of these BZ and TH structure-activity series along with computer-assisted mol. modeling techniques, the authors detd. which chem. structural components were important at the transporter interaction site. By superimposing structures from active chema., excluding residues from poor inhibitors, and incorporating mol. electropotential date, the authors developed a five-point model of BZ conformational similarity to the endogenous transporter ligand, L-T3: the alkyl substitution at the N1 of the BZ ring seems to stimulate the interaction of T3, and the electroproc. halogen and oxygen atoms of

ine
side chain of T3, and the electroneg, halogen and oxygen atoms of
substituents at R3/R7/R2\*/R8\* of BZ form a pyrimidyl pharmacophore that
seems to correspond with the 3-1/5-1/3\*-1/4\*-ON substituents of T3, resp.
These points, suggesting a titled cross-bow formation, may be sites for
ligand interaction with the iodothyronine transporter.
105170-31-8, SKP-L 93216
RL. BIOL (Biological study)
(triodothyronine binding by iodothyronine transporter inhibition by,
structure in relation to)
105170-31-8 CAPLUS
L-Tyrosine, O-(4-hydroxy-3-{(4-hydroxyphenyl)methyl)phenyl}-3,5-diiodo(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Habte

ANSWER 10 OF 20 CAPLUS COPYRIGHT 2003 ACS

L4 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:435024 CAPLUS
TITLE: 121:35024 CAPLUS
TITLE: 21:35024 CAPLUS
Or-methoxyphenylaulfonyl)-3,5-dibromophenylacetic thyromimetic cholesterol-lowering agents
HNVENTOR(S): Walker, Keith A.; Labadie, Sharada S.; Kertesz, Denia J.; Laughton, Craig M.
PATENT ASSIGNEE(S): Syntex (U.S.A.), Inc., USA
U.S., 15 pp.
CODEN: USXXAM
Patent

DOCUMENT TYPE: LANGUAGE:

Patent English

PAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE US 5284971
PRIORITY APPLN. INFO.:
OTHER SOURCE(S):
GI 19940208 US 1992-914837 US 1992-914837 MARPAT 121:35024 A 19940208

Title compds. I (R1 = R9CO(CHNR7R8)m(CH2)n wherein n = 1-3, m = 0,1, R7, R8 = H, C1-4 alkyl, R9 = H0, C1-4 alkoxy, R8R7M; R3, R5 = Br, Cl. iodo, Me; R31 = H, Cl, Br, iodo, C1-4 alkyl, C4-6 cycloalkyl, C1-4 haloalkyl, C4-6 halocycloalkyl, Ar(R10)CH wherein Ar = 5-hydroxypyrida-2-yl, 6-hydroxypyridazin-3-yl, 6-hydroxypyridazin-3-yl, 6-hydroxypyridazin-3-yl, 8-methoxypyridazin-3-yl, 6-hydroxypyridazin-3-yl, N-oxide, R10 = H, C1-4 alkyl; R41 = H0, bioprecursor) and pharmaceutically acceptable salts thereof, useful as anticholesteremic agents (no data), are prepd. SO2C12 in CH2Cl2 was added to Me 3,5-dibromo-4-mercaptophenylacetate (prepn. given) followed by 2-(Me2CH)C6H4OMe to give Me 3,5-dibromo-4-(13-isopropyl-4-methoxyphenyl)thiolphenylacetate which with m-C1C6H4CO2OH in CH2Cl2 was reacted for 20 h to give I (R1 = Me02CCH2, R3 = R5 = Br, R31 = Me2CH, R41 = MeO). Pharmaceutical formulations comprising I are given. 185780-54-4P

155780-54-4P
RL: SFM (Synthetic preparation); PREP (Preparation)
(prepn. of, as anticholesteremic)
155780-54-4 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-{[4-hydroxy-3-[(4-hydroxyphenyl)methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:635049 CAPLUS
TITLE: 111235049 CAPLUS
TITLE: as colorants for near-infrared filters, optical disk memory devices, and liquid crystal devices
MORIBITED RESIDENCE: 1012 AND ACCEST AND ACC

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

PATENT NO. KIND DATE APPLICATION NO. DATE

JP 64000076 A 2 19890105 JP 1987-154333 19870623

PRIORITY APPLN. INFO.: MARPAT 111:235049

GI For diagram(s), see printed CA Issue.
AB The title compde. [I and II; Rl, R3, R5 = H, F, Cl, Br, cyano, Me, Et, MeO, EtO, CF3; R2, R4, R6 = H, F, Cl, Br, cyano, NO2, CF3, nonafluorobutyl, R7, OR7, SR7, S02R7, COR7, (CH2)mCO2R7, NHCO2R7, p-R7C6H4, 4-R7-substituted-cyclohex-1-yl, OR8, provided that both R2 and R4 do not take the same group; R7 = Cl-12 alkyl optionally interrupted by 1-3 O or substituted by cyclohexyl, cyclohexyloxy, Ph, or PhO; R8 = C2-9 alkyl having .gtoreq.3 H's substituted with F; m = 0, 1, 2 having light.

light.

tr., heatr, and chem. stability and good compatibility with synthetic resins, org. solvents, and liq. crystals and useful for near-IR filters, optical disk memory devices using laser beams, and liq. crystal devices for heat-mode recording by laser beam, were prepd. Thus, a mixt. of o-H2NCGH4SH 125, 1,8-dihydroxy-2,7-dibromo-4-(p-n-butylantino)-5-(p-methylamino)anthraquinone 65, and N-methylpyrrolidone 300 parts was

6 h at 195-200.degree. and cooled to 70.degree.. MeOH 500 parts was added

and pptd. crystals were removed by filtration, washed with MeOH and H2O, and dried to give 36 parts II (R1 = R3 = R5 = R6 = H, R2 = Me, R4 = Bu) which had lambds.eax 780 nm and .epsilon. 29 and 900. 134536-61.

RL: USES (Uses)

RL: USES (Usea)
(prepn. of inomeric mixts. contg., as colorants for near-IR filters, optical disk memory devices, and liq. crystal devices)
RN 123658-61-7 CAPLUS
CN Benzeneacetic acid,
4-[[11-{(2-aminophenyl)thio]-13,14-dihydro-12-hydroxy-8,13-dioxo-7-(phenylamino)-8H-naphtho[2,3-a]phenothiazin-9-yl]amino]-, methyl ester (9CI) (CA INDEX NAME)

ANSWER 11 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

ANSWER 12 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

# 10/082,022

L4 ANSWER 13 OF 20
ACCESSION NUMBER:
DOCUMENT NUMBER:
110:115292 CAPLUS
TITLE:
AUTHOR(S):
AUTHOR(S):
CORPORATE SOURCE:
SOURCE:
DOCUMENT TYPE:
LANGUAGE:
CORPORATE SOURCE(S):
CASREACT 110:115292
CASREACT 110:115292

DOCUMENT TYPE: LANGUAGE: OTHER SOURCE(S): GI

HO 
$$\longrightarrow$$
 X  $\longrightarrow$  CH<sub>2</sub>CH (NH<sub>2</sub>) CO<sub>2</sub>H

AB Introduction of specific arylmethyl groups at the 3 -position of the thyroid hormone 3,3',5'-triiodo-1-thyronine (T3), and its known hormonally active derivs., gives liver-selective, cardiac-sparing thyromimetics (e.g., 1, x = 0, S; R = aryl group), with potential utility as plasma cholesterol lowering agents. Correlations between in vivo and in vitro receptor binding affinities show that liver/heart selectivity does not depend on receptor recognition but on penetration or access to receptors in vivo. QSAR studies of the binding data of a series of 20 3'-arylmethyl T3 analogs show that electroneg, groups at the para position increase both

both receptor binding and selectivity in vivo. However, increasing 3'-arylmethyl hydrophobicity increases receptor binding but reduces selectivity. Substitution at ortho and meta poeitions reduces both binding and selectivity. Replacement of the 3,5-iodo groups by halogen

Me maintains selectivity, with 3,5-dibromo analogs in particular having increased potency combined with oral bioavailability. Di-Ph thioether derivs. also have improved potency but are less orally active. At the 1-position, the D enantiomer retains selectivity, but removal of the alpha-amino to give a propionic acid results in loss of selective thyromimetic activity.

105370-33-09 117856-25-09 117896-26-1P
117836-27-29 117896-28-39 117896-39-4P
117917-22-39 117917-23-4P 117917-24-5P or

ANSWER 13 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)
117896-27-2 CAPLUS
L-Tyrosine, 3,5-diidod-0-{4-methoxy-3-{4-methoxy-3-{1-methylethyl]phenyl}-N-(trifluoroacetyl)-, ethyl ester (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

117896-28-3 CAPLUS L-Tyrosine, 3,5-diodo-0-[4-methoxy-3-[(2-methoxyphenyl)methyl]phenyl]-N-[trifluoroacetyl)-, ethyl ester (9CI) (CA INDEX NAME)

117896-29-4 CAPLUS L-Tyrosine, O-[3-{(3-chloro-4-methoxyphenyl)methyl]-4-methoxyphenyl]-3,5-diiodo-N-{trifluoroacetyl}-, ethyl ester (9CI) (CA INDEX NAME)

117917-22-3 CAPLUS L-Tyrosine, O-[3-[(4-cyanophenyl)methyl]-4-methoxyphenyl]-3,5-diiodo-N-(crifluoracetyl)-, methyl ester (9CI) (CA INDEX NAME)

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# Page 15

ANSWER 13 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued) RL: RCT (Reactant): SPN (Synthetic preparation): PREP (Preparation); RACT

Absolute stereochemistry.

117896-25-0 CAPLUS L-Tyronine, 0-(3-(3-fluoro-4-methoxyphenyl)methyl]-4-methoxyphenyl)-3,5-diodo-N-(trifluoroacetyl)-, ethyl ester (9CI) (CA INDEX RAME)

Absolute stereochemistry.

117896-26-1 CAPLUS
L-Tyrosine, 3,5-diiodo-0-(4-methoxy-3-[(4-methoxy-3-methylphenyl)methylphenyl)-N-(trifluoroacetyl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry

L4 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

Absolute stereochemistry.

117917-23-4 CAPLUS L-Tyronine, 3.5-diiodo-0-[4-methoxy-3-((4-nitrophenyl)methyl]phenyl]-N-(trifluoroacetyl)-, methyl ester (9CI) (CA INDEX NAME)

117917-24-5 CAPLUS
L-Tyrosine, 0-{3-{{4-fluorophenyl}methyl}-4-methoxyphenyl}-3,5-diiodo-N-(trifluoroacetyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

117917-26-7 CAPLUS L-Tyrosine, O-[3-[4-(acetylamino)phenyl]methyl]-4-methoxyphenyl]-3,5-diiodo-N-(trifluoroacetyl)-, methyl eater (9CI) (CA INDEX NAME)

L4 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

105170-31-8P 117653-10-8P 117653-11-9P
117653-12-0P 117653-13-1P 117653-14-2P
117653-15-3P 117653-16-4P 117653-17-5P
117653-18-6P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and thyromimetic activity of)
105170-31-8 CAPLUS
L-Tyrosine, O-(4-hydroxy-3-{(4-hydroxyphenyl)methyl]phenyl}-3,5-diiodo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

117653-10-8 CAPLUS L-Tyrosine, O-[3-((4-cysnophenyl)methyl]-4-hydroxyphenyl]-3,5-diiodo-(9C1) (CA INDEX NAME)

Absolute stereochemistry.

117653-11-9 CAPLUS L-Tyrosine, O-(3-[(4-fluorophenyl)methyl]-4-hydroxyphenyl)-3,5-diiodo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 13 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

117653-15-3 CAPLUS L-Tyrosine, O-[3-[(3-fluoro-4-hydroxyphenyl)methyl]-4-hydroxyphenyl)-3,5-diodo-[9CI] (CA INDEX NAME)

Absolute stereochemistry.

117653-16-4 CAPLUS L-Tyrosine, O-[3-[(3-chloro-4-hydroxyphenyl])methyl]-4-hydroxyphenyl]-3,5-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

117653-17-5 CAPLUS L-Tyrosine, O-(4-hydroxy-3-[(4-hydroxy-3-methylphenyl)methyl]phenyl}-3,5-diiodo-(5CI) (CA INDEX NAME)

Absolute stereochemistry.

### Page 16

ANSWER 13 OF 20 CAPLUS COPYRIGHT 2003 ACS

117653-12-0 CAPLUS L-Tyrosine, O-(4-hydroxy-3-{(4-nitrophenyl)methyl]phenyl}-3,5-diiodo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

117653-13-1 CAPLUS L-Tyrosine, O.(3-[(4-eminophenyl)methyl]-4-hydroxyphenyl]-3,5-diiodo-, dihydrobromide (SCI) (CA INDEX NAME)

Absolute stereochemistry.

117653-14-2 CAPLUS L-Tyrosine, O-[4-hydroxy-3-[(2-hydroxyphenyl)methyl]phenyl]-3,5-diiodo-(SCI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

117653-18-6 CAPLUS

CN L-Tyrosine,
O-(4-hydroxy-3-[(4-hydroxy-3-(1-methylethyl)phenyl)methyl]phen
yl)-3,5-diodo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

72469-00-2
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(thyromimetic activity of)
72469-00-2 CAPUS
L-Tyrosine, 0-{4-hydroxy-3-(phenylmethyl)phenyl]-3,5-diiodo- (9CI) (CA INDEX NAME)

L4 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:167902 CAPLUS
DOCUMENT NUMBER: 108:167902 CAPLUS
Synthesis of diphenyl thioether derivatives of peptides and amino acids
HObbs, Doug W.; Still, W. Clark
CORPORATE SOURCE: Dep. Chem., Columbia Univ., New York, NY, 10027, USA
SOURCE: CODEN: TELEAY; ISSN: 0040-4039
JOURNAL
LANGUAGE: OTHER SOURCE(S): CASREACT 108:167902

DOCUMENT TYPE: LANGUAGE: OTHER SOURCE(S): GI

The photochem. SRNI coupling of p-mercaptophenylalanine derivs. with iodotyrosine or iodophenylglycine derivs. gave di-Ph thioethers. Thus, the irradn. of iodotyrosine I and mercaptophenylalanine II with a sunlamp for 1 h in liq. NNI gave thioether III. 11355-79-69 113550-86-59

113850-79-69 113850-88-59
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
113850-79-6 CAPLUS,
L-Tyrogine, N-[[1,1-dimethylethoxy)carbonyl]-3,5-bis[[4-[2-[[[1,1-dimethylethoxy]]]-3,5-bis[[4-[2-[[1,1-dimethylethoxy]]]]-3,5-bis[[4-[2-[[1]]]]]

dimethylethoxy)carbonyl]amino]-3-methoxy-3-oxopropyl]phenyl]thio]-0-methyl, methyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

L4 ANSMER 15 OF 20 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:28334 CAPLUS
TITLE: 108:38334 TAPLUS
TITLE: 3,5-diodo-L-thyronines and quantitative atructure-activity studies of in vitro and in vivo thyromimetic activities in rat liver and heart Leeon, Paul D.; Ellis, David; Emmett, John C.; Shah, Virendra P.; Showell, Graham A.; Underwood, Anthony

CORPORATE SOURCE:

Smith Kline French Res. Ltd., Frythe/Welwyn, AL6 9AR, UK
Journal of Medicinal Chemistry (1988), 31(1), 37-54
CODEN: JMCMAR; ISSN: 0022-2623
JOURNAL
English
CASREACT 108:38334

DOCUMENT TYPE: LANGUAGE: OTHER SOURCE(S): GI

Twenty-nine title compds. I (R = CH2:CH2, ally1, Bu, CH2CH2Ph, CH2OH, etc.) were prepd. by using established methods and by a new route involving manipulation of a 3'-formyl intermediate. In vitro hormone receptor binding (to intact nuclei) and in vivo thyromimetic activity (induction of mitochondrial 3-phosphoglycerate oxidoreductase, GPDH) were measured in rat liver and heart for these new analogs and for the 18 previously reported 3'-substituted 3,5-diodo-L-thyromines. Anal. of the binding date using theor. conformation and quant. structure-affinity methods implies that the 3'-substituent recognition site on the thyroid hormone receptor is hydrophobic and limited in depth to the length of the natural iods substituent, but has sufficient width to accommodate a Ph or cyclohexyl group. Receptor binding is reduced by approx. 10-fold in 3'-acyl derivs. which form strong intramol. acceptor hydrogen bonds with the adjacent 4'-hydroxyl. The compds. showed no differences in their relative affinities for heart and liver nuclei, suggesting that receptors in these tissues are similar. However, the relationships between thyromimetic activity (induction of GPDH) and nuclear binding showed some tissue differences. A high correlation between activity and binding is obsd. for full agonists in the heart, but an equally significant correlation for the liver data is only seen when 3'-substituent bulk (molar refractivity) is included in the anal. These results suggest the possibility that differential tissue penetration or access to receptors may occur in vivo.

11068-02-99 111088-36-99 11089-36-79
RL: RCT (Reactant): SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deblocking of)
11083-02-9 CAPLUS
L-Tyrosine, N-accetyl-3,5-diiodo-0-[4-methoxy-3-(phenylmethyl)phenyl]-, ethyl ester (9C1) (CA INDEX NAME)

# Habte

Page 17

L4 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

113850-86-5 CAPLUS L-Phenylalanine, 4,4'-[[5-(1-amino-2-methoxy-2-oxoethyl)-2-methoxy-1,3-phenylane]bis(thio)]bis(N-[(1,1-dimethylethoxy)carbonyl]-, dimethyl (R) - (9CI) (CA INDEX NAME)

L4 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

Absolute stereochemistry.

111088-36-9 CAPLUS
L-Tyrosine, N-acety1-0-(3-benzoy1-4-methoxyphenyl)-3,5-diiodo-, ethyl ester (9C1) (CA INDEX NAME)

Absolute stereochemistry.

111088-50-7 CAPLUS L-Tyrosine, 3,5-diiodo-O-[4-methoxy-3-(2-phenylethyl)phenyl]-N-(trifluoroscetyl)-, methyl ester (9CI) (CA INDEX NAME)

111087-79-7P 111088-00-7P

111087-79-17 111088-00-79
RE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and thyromimetic activity of)
111087-79-7 CAPUS
L-Tyrosine (0-[4-hydroxy-3-(2-phenylethyl)phenyl]-3,5-diiodo-(9CI) (CA
INDEX NAME)

6/23/2003

ANSWER 15 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

111088-00-7 CAPLUS L-Tyrosine, O-(3-benzoyl-4-hydroxyphenyl)-3,5-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT

72469-00-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(thyromimetic activity of)
72469-00-2 CAPLUS
L-Tyrosine, O-[4-hydroxy-3-{phenylmethyl}phenyl]-3,5-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 16 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued) 9,10-dihydro-1,5-dihydroxy-9,10-dioxo-2,6-anthracenediyl]bis(oxy)|bis-,dibutyl ester (9CI) (CA INDEX NAME)

108578-25-2 CAPLUS
Benzenepropanoic acid,
-[[4-[[4-(heptyloxy]phenyl]amino]-9,10-dihydro1,5-dihydroxy-9,10-dioxo-2,6-anthracenediyl]bis(oxy)]bis-, dibutyl ester
(9CI) (CA INDEX NAME)

Page 18

L4 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1987:215497 CAPLUS DOCUMENT NUMBER: 106:215497 Preparation of anthur 1711LE: Preparation of anthur 1981

Preparation of anthraquinone derivatives as dyes for

INVENTOR (S)

Preparation of anthraquinone derivatives as dyes for liquid crystals Morishita, Yasuyoshi; Matsunaga, Daisaku; Oiso, Shoji Nippon Kayaku Co., Ltd., Japan Jpn. Kokai Tokkyo Koho, 12 pp. CODEN: JKXXAP Patent

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE:

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE JP 62005941 JP 05058621 A2 B4 19870112 JP 1985-291950 19851226 JP 05058621 PRIORITY APPLN. INFO.: GI 19930827 JP 1985-50268 19850315

The title compds. I [when X = H or NH2, Y = OH, R1 = H, R2 = C1, Br, Q; when X = OH, Y = H or NH2, R1 = C1, Br, Q, R2 = H; Z = O, S; R3, R6 = H,

P,

Cl. Br. Me, Et. cyano, MeO. EtO; R4, R7 = H, F, Cl. Br. cyano, CP3, CP3(CP2)3, (substituted) alkyl. (substituted) alkoxy, acyl, acylamino, etc.; R5 = Q), useful as liq. crystal compms. Such as dyes for a guest-host effect liq. crystal display device, are prepd. Heating p-BuC6H4OH 15.8, N-methylpyrrolidone 30, and K2CO3 3 parts at 150.degree.

adding 11.2 parts I (R1 = R5 = Br; R2 = R3 = H; R4 = Bu; X = OH; Y = NH2) and heating at 160.degree. gave 4.2 parts I (R1 = R5 = Q where R6 = H, R7 = Bu; Z = O, R2 = R3 = H; R4 = Bu; X = OH; Y = NH2) (III), whose acetone soln. was blue. The dichroic ratios and solubilities (at 20.degree.) of 11% II with ZLI-1565 (Merck), E-8 (BDH) and ZLI-1840 (Merck) were 10.5 and

ANSWER 16 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-B

108578-39-8 CAPLUS
Benzenebutanoic acid, 4,4'-[[4-amino-5-[[4-dodecylphenyl]amino]-9,10-dihydro-1,8-dihydroxy-9,10-dioxo-2,7-anthracenediyl]bis(oxy)}bis-,dipropyl ester (9Cl) (CA INDEX NAME)

(CH<sub>2</sub>)<sub>11</sub>

L4 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-B

ANSWER 16 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-B

- opr-n

108578-55-8 CAPLUS

Benzenebutanoic acid, 4,4'-[[4-{(4-{heptyloxy})phenyl]amino}-9,10-dihydro-1,8-dihydroxy-9,10-dioxo-2,7-anthracenediyl]bis(oxy)|bis-, dioctyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

L4 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1987:131516 CAPLUS DOCUMENT NUMBER: 106:131516 TITLE: A thyromimetic that decr

AUTHOR (S) :

106:131516
A thyromimetic that decreases plasma cholesterol levels without increasing cardiac activity Underwood, A. H.; Emmett, J. C.; Ellis, D.; Flynn, S. B.; Lesson, P. D.; Benson, G. M.; Novelli, R.;

Pearce.

CORPORATE SOURCE:

SOURCE .

N. J.; Shah, V. P. Smith Kline and French Res. Ltd., Welwyn/Hertfordshire, ALE 9AR, UK Nature (London, United Kingdom) (1986), 324(6096), 425-9 445-9 CODEN: NATUAS; ISSN: 0028-0836 Journal English

DOCUMENT TYPE: LANGUAGE: GI

AB A new class of thyromimetics (agents that mimic the ability of the thyroid hormone T3 [6893-02-3] to decrease plasma cholesterol levels) is described. The most potent of these SKF 194901 (I) [105211-33-2] (as detd. by the induction of mitochondrial cytochrome c3-phosphoglycerate oxidoreductase, [9001-49-4] in heart and liver of hypothyroid rats) was

active as T3 at reducing cholesterol levels and at stimulating liver function but had apprx.0.1% the activity of T3 on heart function. In hypothyroid rate and rate with normal thyroid function, I was also shown to be a potent hypotholesterolemic agent with only a small effect on metabolic rate (detd. by whole body O consumption). The affinities of

thyromimetics for the thyroid hormone receptor of isolated heart and

ruclei were detd., and the relationship between receptor affinity and structure is discussed.
72469-00-2 105170-31-8
RL: BIOL (Biological study)
(as thyromimetic, hypocholesterolemic activity of and heart and liver functions response to, thyroid hormone receptor binding in relation

72469-00-2 CAPLUS L-Tyrosine, O-[4-hydroxy-3-(phenylmethyl)phenyl]-3,5-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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ANSWER 17 OF 20 CAPLUS COPYRIGHT 2003 ACS

L-Tyrosine, O-(4-hydroxy-3-[(4-hydroxyphenyl)methyl]phenyl]-3,5-diiodo-(9CI) (CA INDEX NAME)

L4 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER:
DOCUMENT NUMBER:
1171LE:
INVENTOR(S):
Leason, Paul David; Emmett, John Colin; Underwood,
Anthony Hubert; Ellis, David
Smith Kline and French Laboratories Ltd., UK
EUr. Pat. Appl., 59 pp.
CODEN: EPXXDW
DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,								
			APPLICATION NO.					
EP 188351	A2		EP 1986-300178	19860113				
EP 188351	A3	19890315						
EP 188351		19910313						
R: AT, BE,	CH, DE	, FR, GB,	IT, LI, LU, NL, SE					
AU 8652219	A1	19860724	AU 1986-52219	19860113				
AU 577917	B2	19881006						
AT 61581	E	19910315	AT 1986-300178	19860113				
CA 1319148	A1	19930615	CA 1986-499485	19860113				
US 4766121	Α	19880823	US 1986-818626	19860114				
IL 77605	λl	19900209						
DK 8600185	λ	19860719						
DK 164592		19920720						
DK 164592	c	19921207						
ZA 8600319	Ä	19860827		19860116				
FI 8600229	Ä	19860719		19860117				
NO 8600159	Ä	19860721		19860117				
HU 40401	A2	19861228						
HU 194807	В	19880328						
	A1		ES 1986-551005	19860117				
JP 61167643	A2	19860729		19860118				
JP 07103070	B4	19951108						
CN 86100894	A	19860903		19860118				
CN 1010310	В							
US 4826876			US 1987-136240	19871221				
US 4910305		19900320		19880316				
US 5061798		19911029		19891027				
PRIORITY APPLN. INFO		19911029	GB 1985-1372	19850118				
PRIORITI APPEN. INFO			EP 1986-300178					
			US 1986-818626					
			US 1988-168780					
OTHER SOURCE(S):		CDENCE 10		13000310				
OTHER SOURCE(S):	CA	CARRACI IDS: 403300						

ANSWER 18 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

GI

105170-46-5 CAPLUS L-Tyrosine, -hydroxy-3-[1-(4-hydroxyphenyl)ethyl]phenyl]-3,5-diiodo-N-{trifluoroacetyl}-, ethyl ester (9CI) (CA INDEX NAME)

105170-31-8P 105170-36-3P 105170-42-1P
105170-47-6P
RL: SFN (Synthetic preparation); PREP (Preparation)
(prepn. of, as anticholesteremic)
105170-31-8 CAPLUS
L-Tyrosine, O-[4-hydroxy-3-[{4-hydroxyphenyl}methyl]phenyl]-3,5-diiodo(9CI) (CA INDEX NAME)

RN 105170-36-3 CAPLUS
CN L-Phenylalanine,
4-[(4-hydroxy-3-((4-hydroxyphenyl)methyl]phenyl]thio]-3,5diiodo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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ANSWER 18 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

Acids and deriva. I [R1 = 2-amino-2-carboxyethyl, CO2H, carbalkoxy, carbamoyl, carboxy-, carbalkoxy-, or carbamoylalkyl, etc.; R2 and R3 = H, halo, alkyl, NO2, NH2; Z1 = O, S, CH2; R4 = OH, alkoxy, OCH2Ph, etc.; R5

halo, alkyl; NG2, NH2; 21 = 0, S, CH2; M4 = OH, alkoxy, OCH2PA, etc.; NS

H, alkyl; R6 = 4-HOC6H4, 5-hydroxy-2-pyridyl, 6-oxo-3(1H)-pyridyl),
6-oxo-3(1H)-pyridazinyl] were prepd., and they exhibited
anticholesteremic
activity in rats. A 3,5-dibromotyrosine deriv. was etherified by a
diaryliodonium perchlorate deriv. to give, after deprotection, I [R1 =
CH2CH(NH2)CO2H, R2 = R3 = BF, Z1 = O, R4 = HO, R5 = H, R6 =
6-oxo-3(1H)-pyridyl).

105170-33-0P 105170-41-0P 105170-64-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and deprotection of)
RN 105170-33-0 CAPLUS
CL -Tyrosine, 3,5-diodo-0-[4-methoxy-3-[(4-methoxyphenyl)methyl]phenyl]-N(trifluoroacetyl)-, methyl ester (SCI) (CA INDEX NAME)

Absolute stereochemistry.

105170-41-0 CAPLUS
L-Phenylalanine, 3,5-diiodo-4-([4-methoxy-3-[(4-methoxyphenyl)methyl]phenyl]thio]-N-(trifluoroacetyl)-, ethyl ester (9CI)(CA INDEX NAME)

Absolute stereochemistry.

ANSWER 18 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

105170-42-1 CAPLUS L-Tyrosine, O-[4-hydroxy-3-[1-[4-hydroxyphenyl]ethyl]phenyl]-3,5-diiodo-[GCI] (CA INDEX NAME)

105170-47-6 CAPLUS L-Tyrosine, N-acetyl-O-[4-hydroxy-3-[(4-hydroxyphenyl)methyl]phenyl]-3,5-diiodo- (9CI) (CA INDEX NAME)

# 10/082,022

L4 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1982:466791 CAPLUS
DOCUMENT NUMBER: 97:66791 Chemical structure-biological activity study of the thyroxine binding site of human prealbumin
Simon, 2.: Chiriac, A.; Chiriac, Veronica
Discipl. Biofiz., Inst. Med., Timisoara, Rom.
Timisoara Medicala (1981), 26(3), 26-8
CODEN: TIMEBY; ISSN: 0493-3079
JOURNEL

The T4 (I) [51-48-9] receptor of human prealbumin was studied by the MTD method (Balaban, A. T., et al., 1980) based on binding data for 27 T4 derivs. (Andrea, T. A., et al., 1980). Min. steric differences were calcd. by a variant which allowed for differentation between atoms of the 2nd, 3rd, or higher periods. The structure activity relation with MTD . AB

an indicator variant for the presence of an NH3+ group gave the values of correlation coeff. r=0.95 and std. deviation S=0.71 kcal/mol. These values were in agreement with those obtained by the more complex method

G. M. Crippen (1980).
72469-00-2
RL: PROC (Process)
(prealbumin binding of, in human, structure in relation to)
72469-00-2 CAPUS
L-Tyrosine, O-{4-hydroxy-3-(phenylmethyl)phenyl}-3,5-diiodo-{9CI} (CA

Absolute stereochemistry.

L4 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:
DOCUMENT NUMBER:
1980:52416 CAPLUS
1980:52416 Dinding of thyroid hormones and analogs to the human plasma protein prealbumin
AUTHOR(S):
CORPORATE SOURCE:
Sch. Pharm., Univ. California, San Prancisco, CA, 94143, USA
SOURCE:
Biochemistry (1980), 19(1), 55-63
CODE: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE:
LANGUAGE:
English

DOCUMENT TYPE: LANGUAGE: GI

The relative binding affinities to the human plasma protein prealbumin of the thyroid hormones, L-thyroxine [1] [51-48-9] and L-3,3',5-triiodothyronine [II] [6893-02-3], and of 37 close structural analogs were measured by equil. dialysis. Anal. of the contributions of substituents to binding showed that all 4 iodine atoms contribute favorably. Addn. of an iodine atom to an analog contribute more rably in the outer ring than in the inner ring. Halogen substituents in the 3, 5, and 3' positions contributed more to binding than did alkyl groups

the same hydrophobic character in the same positions. This suggests a H-bonding and(or) charge transfer interaction between the halogen and the protein. An electrostatic interaction between the carboxylate ion of the hormone side chain and the ammonium ion of lysine-15 accounts for the obsd. order in affinities: tetraprop [39846-93-0] > (I and D-thyroxine [51-49-0]) > thyroxxime tight and id D-thyroxine due to an interplay of electrostatic and steric forces involving the lysine-15, leucine-17, and valine-121 residues. The relative contributions of Various structural features of the hormones in binding to presibumin, I-binding globulin, and rat liver nuclear receptor were compared. Strong similarities were obsd. in the features of the 3 and 5 positions and in the side chains in contributing binding affinity

prealbumin and to the receptor. Binding to I-binding globulin and to prealbumin was influenced favorably by the same 3' and 5' substituents. In contrast, binding to the nuclear receptor was enhanced by 3' alkyl and halogen substituents but was decreased by 5' substitution.

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### Page 21

ANSWER 19 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued)

ANSWER 20 OF 20 CAPLUS COPYRIGHT 2003 ACS (Continued) 72469-00-2
RL: PROC (Process)
(prealbumin binding of, structure in relation to) 72469-00-2 CAPLUS
L-Tyrosine, 0-[4-hydroxy-3-(phenylmethyl)phenyl]-3,5-diiodo-(9CI) (CA INDEX NAME)

Page 22

10/082,022

=> log y COST IN U.S. DOLLARS FULL ESTIMATED COST	SINCE FILE ENTRY 91.14	TOTAL SESSION 239.90
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-13.02	-13.02

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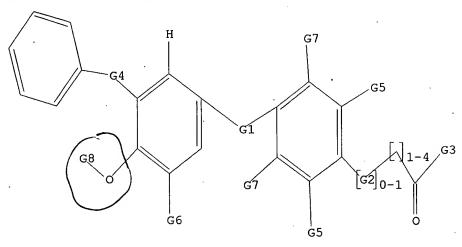
Uploading 10082022.str

# L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS

L1 STE



Page 3

G1 O, S, N, CH2, CH, CF2, SO2, NH

G2 O, S

G3 O, N

G4 C, S, N, CH, CF2, Ak

G5 H, Et, n-Pr, i-Pr, n-Bu, i-Bu, s-Bu, t-Bu, Me

G6 H, Me, Et, n-Pr, i-Pr, n-Bu, i-Bu, s-Bu, t-Bu, Ak, X

- G7 H, CN, X, Cb, Ak, CH2, CH, CF2, CF3

G8 H,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 09:37:43 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 8232 TO ITERATE

12.1% PROCESSED 1000 ITERATIONS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS:

159205 TO 170075

PROJECTED ANSWERS:

0 TO

L2 0 SEA SSS SAM L1

=> s 11 sss full

6/23/2003

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0 ANSWERS

10/082,022 Page 4

FULL SEARCH INITIATED 09:37:53 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 164456 TO ITERATE

100.0% PROCESSED 164456 ITERATIONS **SEARCH TIME: 00.00.06** 

62 ANSWERS

L3

62 SEA SSS FUL L1

=> file caplus COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

148.55

148.76

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FILE COVERS 1907 - 25 Jun 2003 VOL 138 ISS 26 FILE LAST UPDATED: 24 Jun 2003 (20030624/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification. The second secon

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15 L3

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L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2003:173554 CAPLUS DOCUMENT NUMBER: 138:221353

DOCUMENT NUMBER: TITLE: 138:221353
Preparation of aryloxyphenols as thyroid receptor antagonists for the treatment of cardiac and metabolic

clsorders
Malm, Johans Brandt, Peters Edvinsson, Karins Koehler,
Konrad: Sanin, Andreis Gordon, Sandra
Karo Bio AB, Swed.
PCT Int. Appl., 42 pp.
CODEN: PIXXO2
PSTANT INVENTOR(S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

WO 2003018515 A2 20030306 WO 2002-EP9120 20020813

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, II, IN, IS, DP, KE, KG, KP, KR, KZ, LC, LK, LL, LX, LT, LU, LV, HA, MD, MG, MK, MM, MY, MZ, MZ, NO, NZ, CM, PH, PL, PT, NO, RU, SD, SE, SG, SI, SK, SI, TJ, TM, TM, TR, TT, TJ, UA, UG, US, UZ, VN, YU, ZA, ZH, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO:

GB 2001-20691 A 2002001

GB 2001-20691 GB 2002-7719 MARPAT 138:221353

OTHER SOURCE(S):

L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

ble bond geometry as shown.

500794-95-6 CAPLUS
Benzenepropanoic acid, 3,5-dibromo-4-[3-[(1E)-2-[4-[(dimethylamino)methyl]phenyl]-4-hydroxy-5-(1-methylethyl)phenoxy]-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

500794-97-8 CAPLUS Senzenepropanoic acid, 3,5-dibromo-4-[3-[(1E)-2-(4-carboxyphenyl)ethenyl]-4-hydroxy-5-(1-methylethyl)phenoxy]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

500795-00-6 CAPLUS Benzenepropanoic acid, 3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)-5-(2-phenylethyl)phenoxy]- (9CI)- (CA INDEX NAME)

Page 5

ANSWER 1 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

Title compds. I [R1 = carboxy, ester. .alpha.-hydroxycarboxy, etc.: R2-3 = Cl. I. Br. alkyl. haloalkyl. alkenyl. etc.: R4 = halo, alkyl. alkenyl. alkynyl. etc.: X = CH2CH2. CH2CH2. CH=CH, etc.: R5 = (hetero)aryl. cycloalkyl. etc.: x = O+22 are prepd. For instance, M = (hetero)aryl. cycloalkyl. etc.: x = O+22 are prepd. For instance, M = (hetero)aryl. gycloalkyl. etc.: x = O+22 are prepd. For instance, M = (hetero)aryl. gycloalkyl. etc.: x = O+22 are prepd. For instance, M = (hetero)aryl. gycloalkyl. etc. x = (hetero)aryl. gycloalkyl. gy

(Uses)
(aryloxyphenols as thyroid receptor antagonists for treatment of cardiac and metabolic disorders)
500794-84-3 CAPLUS
Benzenepropanoic acid, 3,5-dibromo-4-[4-hydroxy-3-(1-methylethyl)-5-[(1E)-2-phenylethenyl)phenoxyl- (9CI) (CA INDEX NAME)

ANSWER 1 OF 15 CAPLUS COPYRIGHT 2003 ACS

500795-02-8 CAPLUS
Benzenepropanoic acid, 3,5-dibromo-.alpha.-hydroxy-4-[4-hydroxy-3-(1-methylethyl)-5-[(1E)-2-phenylethenyl]phenoxy]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c} Ph & \stackrel{E}{\underset{1-Pr}{\longleftarrow}} OH \\ & \\ & \\ & \\ \end{array}$$

500795-11-9 CAPLUS
Benzenepropanoic acid, 3,5-dibromo-.alpha.-hydroxy-4-[4-hydroxy-3-(1-methylethyl)-5-(2-phenylethyl)phenoxy]- (9CI) (CA INDEX NAME)

500795-01-7P, Methyl (E)-3-[3,5-dibromo-4-[4-hydroxy-3-isopropyl-5-(2-phenylethenyl)phenoxy]phenyl]propionate 500795-08-4P, Methyl (E)-3-[3,5-dibromo-4-[4-hydroxy-3-isopropyl-5-(2-phenylethenyl)phenoxy]phenyl]-2-hydroxypropionate 500795-12-0P, Methyl 3-[3,5-dibromo-4-[4-hydroxy-3-isopropyl-5-(phenethyl)phenoxy]phenyl]-2-hydroxypropionate RL: RCT (Reactant): SPN (Synthetic preparation): PREP (Preparation): RACT (Reactant or reagent) (aryloxyphenols as thyroid receptor antagonists for treatment of cardiac and metabolic disorders) 500795-01-7 CAPLUS Benzenepropanoic acid, 3,5-dibromo-4-[4-hydroxy-3-[1-methylethyl]-5-[(1E)-2-phenylethenyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

500795-08-4 CAPLUS Benzenepropanoic acid, 3,5-dibromo-.alpha.-hydroxy-4-[4-hydroxy-3-[1-methylethyl]-5-[(1E)-2-phenylethenyl]phenoxy]-, methyl ester (9CI) (INDEX NAME)

Double bond geometry as shown.

$$\begin{array}{c} \text{Ph} & \\ \\ \text{HO} & \\ \\ \text{i-Pr} & \\ \end{array} \\ \begin{array}{c} \text{Br} \\ \\ \text{OH} \\ \\ \end{array} \\ \begin{array}{c} \text{OMe} \\ \\ \end{array}$$

500795-12-0 CAPLUS

Benzenepropanoic acid, 3,5-dibromo-.alpha.-hydroxy-4-[4-hydroxy-3-(1-methylethyl)-5-(2-phenylethyl)phenoxy]-, methyl ester (9CI) (CA INDEX

$$\begin{array}{c} \text{Ph-CH}_2\text{-CH}_2 \\ \text{HO} \\ \text{i-Pr} \end{array} \begin{array}{c} \text{Br} \\ \text{CH}_2\text{-CH-C-OMe} \end{array}$$

L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

Page 6

L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER:
DOCUMENT NUMBER:
138:280956
A thyroid hormone antagonist that inhibits thyroid
hormone action in vivo
Lim, Waylandi Nguyen, Ngoc-Ha; Yang, Ha Yung; Scanlan,
Thomas S.; Furlow, J. David
Sect. Neurobiol., Physiol, Behavior, University of
California, Davis, CA, 95616-8519, USA
JOURNEL OF BOOGLES JOURNEL OF BOOGLES ABERTAL
PUBLISHER:
American Society for Biochemistry and Molecular
Biology

Biology Journal DOCUMENT TYPE:

MENT TYPE: Journal

UAGE: English

We have characterized the newly developed thyroid hormone antagonist NH-3
in both cell culture and in vivo model systems. NH-3 binds Xenopus laevis
thyroid hormone receptors directly in vitro and induces a conformation
distinct from agonist-bound receptors. Transcriptional activation of a
thyroid hormone response element-conty, reporter gene is strongly
inhibited by NH-3 in a dose-dependent manner. In addn., NN-3 prevents X.
laevis thyroid hormone receptors from binding to the pl60 family of
co-activators GRIP-1 and SRC-1 in a two-hybrid assay. To assess the
potency of the compd. in vivo, we used induced and spontaneous X. laevis
tadpole metamorphosis, a thyroid hormone-dependent developmental process.
NH-3 inhibits thyroid hormone-induced morphol. changes in a dose-dependent
manner and inhibits the up-regulation of endogenous thyroid
hormone-responsive genes. Spontaneous metamorphosis is efficiently and
reversibly arrested by NH-3 with at least the same effectiveness as the
thyroid hormone synthesis inhibitor methimazole. Therefore, NH-3 is the
first thyroid hormone antagonist to demonstrate potent inhibition of
thyroid hormone action in both cell culture- and whole animal-based
assays.

44/415-20-1
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action);
PAC (Pharmacological activity); BIOL (Biological study)
. (thyroid hormone antagonist that inhibits thyroid hormone action in

(tnyroid hormone antagonist that inhibits thyroid hormone action in vivo)
47415-26-1 CAPLUS
Acetic acid, [4-[[4-hydroxy-3-(1-methylethyl)-5-[(4-nitrophenyl)ethynyl]phenyl]methyl]-3,5-dimethylphenoxy]- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2002:716241 CAPLUS DOCUMENT NUMBER: 137:232450 TITLE: Preparation of the control of the contro

137:232450
Preparation of biphenyl derivatives as thyroid hormone analogs
Haning, Helmut, Woltering, Michael; Schmidt, Gunter; Faeste, Christiane; Bischoff, Hilmar; Kretschmer, Axel; Voehringer, Verena; Ellinghaus, Peter INVENTOR (S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

	PAT	ENT	NO.		KI	ND	DATE			A	PPLI	CATI	ON N	ο.	DATE			
										-								
	WO	200	2072	539	A	1	2002	0919		౪	0 20	02-E	P206	5	2002	0227		
		W:	AE.	. AG.	AL.	AM.	AT.	AU.	AZ.	BA.	BB.	BG.	BR.	BY.	BZ.	CA,	CH,	CN,
			CO	CR,	CU,	CZ,	DE,	DK,	DM.	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
			GM.	, HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
			LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
			PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	sĸ,	SL,	ΤJ,	TM,	TN,	TR,	TT,	ŤZ,
			UA.	, UG,	US,	υz,	VN,	YU,	ZA,	ZM,	ZW,	AM,	AZ,	BY,	KG,	ΚZ,	MD,	RU,
			TJ.	, TM														
		RW	: GH	, GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	ΑT,	ΒE,	CH,
			CY.	, DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,
			BF.	, BJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
	DE	101	3083	5	A	1	2002	0919		D	E 20	01-1	0130	835	2001	0627		
	บร	200	3105	078	A	1	2003	0605		U	S 20	02-8	2022		2002	0226		
RIOI	RITY	' AP	PLN.	INFO	.:					DE 2	001-	1011	1651	A	2001	0312		
											001	1012	0025		2001	0637		

OTHER SOURCE(S): MARPAT 137:232450

Title compds. [I; X = 0, S, SO2, CH2, CHF, CF2, NR8; R8 = H, alkyl; R1, R2 = H, alkyl; R3, R4 = H, halo, cyano, alkyl, CF3, CH2F, Vinyl, cycloalkyl; R5 = H, alkyl, halo; R6 = SR9, S(0)nR10, NR11c(0)R12, CH2, ctc.: R9 = alkyl, cycloalkyl, alkenyl, acyl, arylnethyl, etc.: n = 1, 2; R10 = OR15, NR16R17, alkyl, cycloalkyl, etc.: R15 = H, Ph, benzyl, alkyl, etc.: R16, R17 = H, (branched) (substituted) alkyl, etc. R11 = H, (branched) (substituted) alkyl, etc. R11 = H, (branched) (substituted) alkyl, etc.; R7 = H, alkyl, alkanoyl; Z = YmWCOR36; Y = O, S; m = 0, 1; W = (substituted) alkylene: R36 = OR37, NR38R39: R37-R39 = H, Ph, benzyl, alkyl, etc.], were prepd. as thyroid hormone analogs (no data). Thus, Et (4-(4-[beryloxyl]-3-[(4-fluorophenyl])sulfonyl]benzyl)-3,5-dimethylphenoxyl) acetate (prepn. given) in EtOH was hydrogenated in the

6/23/2003

ANSWER 3 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued) presence of Pd/activated C for 2 h at room temp. and 1013 mbar to give 86t Et [4-(3-[(4-fluorophenyl)]sulfonyl]+4-hydroxybenzyl]-3,5-0 dimethylphenoxyl actate which was sapond. with 1 N MaOH in EtOH to give 900 [4-(3-[(4-fluorophenyl)]sulfonyl]-4-hydroxybenzyl]-3,5-0 dimethylphenoxyl actic acid. The compds. 1 are esp. sultable for use in any indications that may be treated with natural thyroid hormones such as depression or thyroid tumor. The inventive compds. I are preferably used to treat arteriosclerosis, hypercholesterolenia, dyslipidemia as well as obesity.
459431-01-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic

459431-01-7P
RL: PAC (Phermacological activity); RCT (Reactant); SPN (Synthetic preparation); TRU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (prepn. of biphenyl derivs. as thyroid hormone analogs) 459431-01-7 CAPLUS Acetic acid, [4-[13-[4-fluorophenyl]sulfonyl]-4-hydroxyphenyl]methyl]-3,5-dimethylphenoxy]-, ethyl ester (9CI) (CA INDEX NAME)

459431-02-8P 459431-03-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of biphenyl derivs. as thyroid hormone analogs) 459431-02-8 CAPLUS
Acetic acid, [4-[13-[(4-fluorophenyl)sulfonyl]-4-hydroxyphenyl]methyl]-3,5-dimethylphenoxy]- (9CI) (CA INDEX NAME)

459431-03-9 CAPLUS Propanoic acid, 2-[4-[[3-[(4-fluorophenyl)sulfonyl]-4-hydroxyphenyl]methyl]-3,5-dimethylphenoxy]-2-methyl- (9CI) (CA INDEX NAME)

ANSWER 3 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT REFERENCE COUNT:

L4 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2003 ACS

459430-99-0F 459431-00-6F
RL: RCT (Reactant): SFN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of hiphenyl derivs. as thyroid hormone analogs)
459430-99-0 CAPLUS
Acetic acid, [4-[[3-[(4-fluorophenyl]sulfonyl]-4(phenylmethoxy)phenyl]methyl]-3,5-dimethylphenoxy)-, ethyl ester (9CI)
(CA INDEX NAME)

(Continued)

459431-00-6 CAPLUS
Propanoic acid, 2-(4-[[3-([4-fluorophenyl]sulfonyl]-4-(phenylmethoxy)phenyl]methyl]-3,5-dimethylphenoxy]-2-methyl-, ethyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 15
ACCESSION NUMBER:
DOCUMENT NUMBER:
137:165293
Rational Design and Synthesis of a Novel Thyroid
Hormone Antagonist That Blocks Coactivator Recruitment
Nguyen, Ngoc-Har Apriletti, James W., Lima, Suzana T.
Cunhar Webb, Paul: Baxter, John D.: Scanlan, Thomas S.
Program in Chemistry and Chemical Biology, Departments
of Pharmacology, University of California, San Francisco,
CA, 94143-0446, USA
Journal of Medicinal Chemistry (2002), 45(15),
3310-3320
COEN: JMCMAR; ISSN: 0022-2623
American Chemical Society
Journal LANGUAGE:

FUBLISHER:
DOCUMENT TYPE:
Journal
LANGUAGE:
English

CAPLUS
COPYRIGHT 2003 ACS
2002:457917
CAPLUS
137:165293
Rational Design and Synthesis of a Novel Thyroid
Hormone Antagonist That Blocks Coactivator Recruitment
Nguyen, Ngoc-Har Apriletti, James W., Lima, Suzana T.
Cunhar Webb, Paul: Baxter, John D.: Scanlan, Thomas S.
Program in Chemistry and Cellular, and-Molecular;
Pharmacology, University of California, San Francisco,
CA, 94143-0446, USA
Journal of Medicinal Chemistry (2002), 45(15),
3310-3320
COEN: JMCMAR; ISSN: 0022-2623
American Chemical Society
Journal
LANGUAGE:

PUBLISHER: DOCUMENT TYPE: LANGUAGE: OTHER SOURCE(S): GI English CASREACT 137:169293

The authors report the design and synthesis of a novel series of phenylethynyl derivs. I [R = H, (CH2)4Me, NO2, NH2] sharing the halogen-free thyronine scaffold of GC-1 (II). I (R = NO2) is a T3 antagonist with negligible TR agonist activity and improved TR binding affinity and potency that allow for further characterization of its obadactivity. Its ability to block TR-coactivator interactions appears to be the mechanism for antagonism. It will be a useful pharmacol. tool for further study of T3 signaling and TR function.
447415-19-29 447415-22-7P 447415-26-1P
447415-29-4P
HL: BSU (Biological study, unclassified): SPN (Synthetic preparation):
BIOL (Biological study): PREP (Preparation)
(prepn. of phenylethynyl derivs. of GC-1 as thyroid hormone analogs and their binding activity towards thyroid hormone receptors)
447415-19-2 CAPLUS
Acctic acid, [4-[4-hydroxy-3-(1-methylethyl)-5(phenylethynyl)phenyl]methyl]-3,5-dimethylphenoxy)- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

447415-22-7 CAPLUS
Acetic acid, [4-[(4-hydroxy-3-(1-methylethyl)-5-[(4-pentylphenyl)ethynyl]phenyl]methyl]-3,5-dimethylphenoxy]- (9CI) (CA INDEX NAME)

447415-26-1 CAPLUS
Acetic acid, [4-[4-hydroxy-3-(1-methylethyl)-5-[(4httrophenyl)ethynyl]phenyl]sethyl]-3,5-dimethylphenxy]- (9CI) (CA INDEX

447415-29-4 CAPLUS
Acetic acid, [4-[3-[(4-aminophenyl)ethynyl]-4-hydroxy-5-(1-methylethyl)phenyl]methyl]-3,5-dimethylphenoxy)- (9CI) (CA INDEX NAME)

IT 446312-33-0P 446312-34-1P 446312-36-3P

PL'scular .

ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued) 446312-37-4 CAPLUS Acetic acid, [4-[(3-{(4-aminophenyl)ethynyl]-4-(methoxymethoxy)-5-(1-methylethyllphenyl]methyl]-3,5-dimethylphenoxy]-, methyl ester (9CI) (CA INDEX NAME)

$$\bigcap_{\substack{0\\ \text{MeO-C-CH}_2-0}}^{\text{Me}} \bigcap_{\substack{\text{Me}\\ \text{i-Pr}}}^{\text{NH}_2} \bigcap_{\text{O-CH}_2-\text{OMe}}^{\text{NH}_2}$$

446312-38-5 CAPLUS Acetic acid, [4-[[4-[methoxymethoxy]-3-(1-methylethyl]-5-[(4-nitrophenyl]ethynyl]phenyl]methyl]-3,5-dimethylphenoxy]-, methyl ester (9CI) (CA INDEX NAME)

$$\underset{\mathsf{MeO-C-CH}_2-\mathsf{O}}{\overset{\mathsf{Me}}{\bigcirc}} \overset{\mathsf{Me}}{\underset{\mathsf{i-Pr}}{\bigcirc}} \overset{\mathsf{No}}{\underset{\mathsf{i-Pr}}{\bigcirc}} \overset{\mathsf{No}}{\underset{\mathsf{i-Pr}}{\overset{\mathsf{i-Pr}}{\longrightarrow}} \overset{\mathsf{No}}{\underset{\mathsf{i-Pr}}{\bigcirc}} \overset{\mathsf{No}}{\underset{\mathsf{i-Pr}}{\longrightarrow}} \overset{\mathsf{No}}{\overset{\mathsf{i-Pr}}{\longrightarrow}} \overset{\mathsf{No$$

446312-39-6 CAPLUS Acetic acid, [4-[[4-hydroxy-3-(1-methylethyl)-5-[(4-nitrophenyl)ethynyl]phenyl]methyl]-3,5-dimethylphenoxy]-, methyl ester (9CI) (CA INDEX NAME)

$$\mathsf{MeO-C-CH_2-O} \overset{\mathsf{Me}}{\underset{\mathsf{i-Pr}}{\bigvee}} \mathsf{CH_2} \overset{\mathsf{CH_2}}{\underset{\mathsf{i-Pr}}{\bigvee}} \mathsf{OH}$$

446312-40-9 CAPLUS
Acetic acid, {a-{[3-[(4-aminophenyl)ethynyl]-4-hydroxy-5-(1-methyltehyl)phenyl]methyl]-3,5-dimethylphenoxy]-, methyl ester (9CI) (CA INDEX NAME)

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#### Page 8

ANSYER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)
446312-37-4P 446312-38-5P 446312-39-6P
446312-40-9P
REL: RCT (Reactant): SPN (Synthetic preparation): PREP (Preparation): RACT
(Reactant or reagent)
(prepn. of phenylethynyl derivs. of GC-1 as thyroid hormone analogs and
their binding activity towards thyroid hormone receptors)
466312-33-0 CAPLUS
Acetic acid. (4-[(4-(methoxymethoxy)-3-(1-methylethyl)-5(phenylethynyl)phenyl]methyl]-3,5-dimethylphenoxy)-, 1,1-dimethylethyl
ester (9CI) (CA INDEX NAME)

446312-34-1 CAPLUS
Acetic acid, [4-[[4-(methoxymethoxy)-3-(1-methylethyl)-5-[(4-pentylphenyl)ethynyl]phenyl]methyl]-3,5-dimethylphenoxy]-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

446312-36-3 CAPLUS
Acetic acid, {4-[{4-hydroxy-3-{1-methylethyl}-5-{4-pentylphenyl}ethynyl]phenyl]methyl}-3,5-dimethylphenoxy}-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT REFERENCE COUNT:

```
L4 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2000:117013 CAPLUS DOCUMENT NUMBER: 132:166010
                                                                132:166010
Preparation of 4-phenoxyphenylacetic acids as glucocorticoid and thyroid hormone receptor ligands for the treatment of metabolic disorders Apelqvist, Theresa: Goede, Patrick: Holmgren, Erik Karo Bio AB, Swed.
PCT Int. Appl., 56 pp.
CODEN: PIXX02
Patent
Facilish
 INVENTOR(S):
PATENT ASSIGNEE(S):
SOURCE:
 DOCUMENT TYPE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
             PATENT NO.
                                                          KIND DATE
                                                                                                               APPLICATION NO. DATE
```

SI 1999-20064 19990804
JP 2000-563607 19990804
AT 1999-936913 19990804
BG 2001-105214 20010202
NO 2001-610 20010205
US 2001-744865 20010409
GB 1998-16935 A 19980005
WO 1999-1B1447 W 19990804 OTHER SOURCE(S): MARPAT 132:166010

L4 ANSWER 6 OF 15
ACCESSION NUMBER:
DOCUMENT NUMBER:
1996:629766 CAPLUS
125:261263
Positive-working resists containing
t-butoxycarbonylmethyloxybenzene dissolution inhibitor
for suppressed alkaline impurity
Watanabe, Atsushi; Ishihara, Toshinobu; Yaqihashi,
Fujio; Tanakı, Haruyori; Kawai, Yoshio; Nakamura, Jiro
Shinetsu Chem Ind Co, Japan; Nippon Telegraph &
Telephone
DOCUMENT TYPE:
DOCUMENT TYPE:
Patent

Paten DOCUMENT TYPE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE ....on NC 2360730 JP 1995-20958 JP 1995-20958 MARPAT 125:261263 JP 08194313 PRIORITY APPLN. INFO.: A2 19960730 OTHER SOURCE(S):

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

TRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

The pos. resists comprise 3 components of an acid generator, a polymer compd., and a dissoln. inhibitor selected from 1,4-bis|bis|4-t-butoxycarbony|nethyloxypheny|nethyl|barcene, its deriv. I [R1-2 = alkyl: k = 0-4; l = 0-2, k + 1 .ltoreq.4), 1,3-bis|4-t-butoxycarbony|nethyloxypheny|nethyl|-4,5-bis-t-butoxycarbony|nethyloxypheny|nethyl-4,5-dimethyl-4,beny|nethyl-4+butoxycarbony|nethyloxypheny|nethyl-2,5-dimethyl-4,beny|nethyl-4+butoxycarbony|nethyloxypheny|nethyloxypheny|propane, its deriv. IV [R4 = alkyl: m = 0-3), 2,6-bis|(2-t-butoxycarbony|nethyloxypheny|nethyloxypheny|nethyl-1-t-butoxycarbony|nethyloxy-4-methylbenzene, and its deriv. V [R4 = alkyl: n = 0-3), 2,6-bis|(2-t-butoxycarbony)nethyloxypheny|nethyl-1-t-butoxycarbony|nethyloxy-4-methylbenzene, and its deriv. V [R4 = alkyl: n = 0, 1; m = 0-(4-n)). The dissoln. inhibitor suppresses penetration of an alk. impurity in the resist film and provides high-resoln. images.

182216-21-3 182216-26-8 182261-28-5
RL: TPM (Technical or engineered material use): USES (Uses)
(pos. resists contp. t-butoxycarbony|methyloxybenzene dissoln. inhibitor for suppressed alk. impurity)

182216-21-3 CAPLUS
Acetic acid; 2,2'-[[4,6-bis[2-(1,1-dimethylethoxy)-2-oxoethoxy]-1,3-phenylene|bis(methylene-4,1-phenyleneoxy)]bis-, bis(1,1-dimethylethyl)

ester (9CI) (CA INDEX NAME)

ANSWER 5 OF 15 CAPLUS COPYRIGHT 2003 ACS

The title compds. [I; Rl = alkyl, aryl, CO2H, etc.; R2, R3 = H, halo, alkyl, etc. (at least one of R2 and R3 being other than hydrogen): X = CO, CH2; R4 = alkyl, aryl, heteroaryl; R5 = halo, alkyl, cycloalkyl; Y = OH, OME, NH2, alkylamino; n = 0-41, useful for treating diseases assocd. with metab. dysfunction or which are dependent on the expression of a glucocorticoid or thyroid receptor gene (such as diabetes, hypercholesterolemia, or obesity) (no data), were prepd. E.g., a multi-step synthesis of ester I [Rl = COZMe; n = 1; R2 = R3 = Br; Y = OMe; R4 = Ph; X = CO; R5 = iso-Pr] was given. Compds. I are effective at 0.5-25 mg/ks/day. 258819-66-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIO, (Biological study); PREP (Preparation); USES (Uses) (prepn. of 4-phenoxyphenylacetic acids as glucocorticoid and thyroid hormone receptor ligands for the treatment of metabolic disorders) 258819-64-6 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-(4-hydroxy-3-(1-methylethyl)-5-(phenylmethyl) phenoxyl- (9CI) (CA INDEX NAME)

258920-36-9
RL: RCT (Reactant): RACT (Reactant or reagent)
(preph. of 4-phenoxyphenylacetic acids as glucocorticoid and thyroid
hormone receptor ligands for the treatment of metabolic disorders)
258920-36-9 CAPLUS
Benzeneacetic acid, 3,5-dibromo-4-[4-methoxy-3-(1-methylethyl)-5(phenylmethyl)phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Ph-CH}_2 \\ \text{MeO} \\ \text{$i-Pr$} \end{array} \\ \text{Br} \\ \begin{array}{c} \text{O} \\ \text{CH}_2 - \text{C-OMe} \end{array}$$

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT 2

182216-26-8 CAPLUS
Acetic acid, 2,2'-[[4,6-bis[2-(1,1\_dimethylethoxy)-2-oxoethoxy]-5-methyl1,3-phenylene]bis[methylene-4,1-phenyleneoxy]]bis-, bis[1,1-dimethylethyl]
ester (9CI) (CA INDEX NAME)

$$\begin{array}{c} 0 \\ CH_2 \\ CH_2$$

182261-28-5 CAPLUS
Acetic acid, 2,2'-[[4-(2-(1,1-dimethylethoxy)-2-oxoethoxy]-1,3-phenylene]bis[methylene(2,5-dimethyl-4,1-phenylene)oxy]]bis-,bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

L4 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1996:628058 CAPLUS DOCUMENT NUMBER: 125:261266 -

DOCUMENT NUMBER: TITLE:

1.3-Bis (4-tert-butoxycarbonylmethyloxyphenylmethyl)-4,6-bis-tert-butoxycarbonylmethyloxybenzene derivative for dissolution inhibitor of three-component resist Watanabe, Atsushi: Ishihara, Toshinobu: Yagihashi,

19950113

INVENTOR(S):

PATENT ASSIGNEE(S): SOURCE:

Fujio
Shinetsu Chem Ind Co, Japan
Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXAF
Patent

ANGUAGE:

DOCUMENT TYPE:

FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE Jou NO JP 1995-20954 JP 1995-20954 MARPAT 125:261266 A2 19960730

JP 08193053 PRIORITY APPLN. INFO.: OTHER SOURCE(S):

t BuO2CCH2O OCH2CO2<sup>t</sup> Bu OCH2CO2<sup>t</sup> Bu t BuO2CCH2C

The deriv. is I (R = H, alkyl). The deriv. shows good soly. toward macromol. compd. in a three-component pos.-working resist, and is useful for dissoln. inhibitor of the resist. 18226-21-39 18226-26-89

182216-21-3P 182216-26-8P
RL: RNU (Preparation, unclassified); TEM (Technical or engineered material use); PREP (Preparation); USES (Uses)
(prepn. of bis(catbonylmethyloxyphenylmethyl)benzene deriv. for dissoln. inhibitor of three-component resist)
182216-21-3 CAPLUS
Acctic acid. 2, 2'-[[4,6-bis[2-(1,1-dimethylethoxy)-2-oxoethoxy]-1,3-phenylene]bis(methylene-4,1-phenylene)bis(methylene-4,1-phenylene)component resist)
ester (9CI) (CA INDEX NAME)

ANSWER 8 OF 15 CAPLUS COPYRIGHT 2003 ACS SSION NUMBER: 1994:450249 CAPLUS MENT NUMBER: 121:50249 ACCESSION NUMBER:

DOCUMENT NUMBER:

TITLE: Computer-assisted molecular modeling of benzodiazepine and thyromimetic inhibitors of the HepG2 iodothyronine

and thyronimetic inhibitors of the Hebez Loodinyronime
membrane transporter
AUTHOR(S): Kragie, Laura; Forrester, Maureen L.; Cody, Vivian;
McCourt, Mary
CORPORATE SOURCE: 
SOURCE: Molecular Endogrinology (1994); 78 (3), 382-91
CODEN: MOENEN; ISSN: 0888-8809

DOCUMENT TYPE:

CODEN: MOREN; ISSN: 0888-8809

UNENT TYPE: Journal

CODEN: MOREN; ISSN: 0888-8809

INCOMEN: TYPE: Journal

CODEN: MOREN; ISSN: 0888-8809

To callular uptake is inhibited in the presence of benzodiazepines (BZs). The structure-activity relationship of BZ inhibition correlates strongly with halogen substitution of the nonfused Ph ring and indicates that this ring is required for activity. A structure-activity series of thyrominetic (TH) inhibitors of the Hep62 Lodothyronine transporter further point out the crit. importance of the amino group of the alanine side chain, its L-stereo configuration, and the size of the substituents of the inner and outer Ph rings. A third series of compds., reported to interact at related sites, were inactive as Hep62 lodothyronine transport inhibitors, and therefore the potent inhibitors were restricted to the BZ and TH structure-activity series along with computer-assisted mol. modeling techniques, the authors detd. which chem. structural components were important at the transporter interaction site. By superimposing structures from active chems., excluding residues from poor inhibitors, and incorporating mol. electropotential data, the authors developed a five-point model of BZ conformational similarity to the endogenous transporter ligand, L-T3: the alkyl substitution at the N1 of the BZ ring seems to stimulate the alanine side chain of T3, and the electrones, halogen and oxygen atoms of substituents at R3/R7/R2/R4' of BZ form a pyrimidyl pharmacophore that seems to correspond with the 3-1/5-1/3-1/4'-OH substituents of T3, resp. These points, suggesting a tilted cross-bow formation, may be sites for ligand interaction with the indothyronine transporter inhibition by, structure in relation to)

105170-31-8 CRPLUS

L-Tyrosine, O-[4-hydroxy-3-[(4-hydroxyphenyl)methyl]phenyl]-3,5-diiodo-(9C1) (CA INDEX NAME)

Absolute stereochemistry.

Page 10

ANSWER 7 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

- OBu-t t - BuO

182216-26-8 CAPLUS
Acetic acid, 2,2'-[[4,6-bis[2-(1,1-dimethylothoxy)-2-oxocthoxy]-5-methyl1,3-phenylene]bis(methylone-4,1-phenyleneoxy)]bis-, bis(1,1-dimethylothyl)
ester (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 15
ACCESSION NUMBER:
1994:435024 CAPLUS
121:35024
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DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

KIND DATE APPLICATION NO. US 5284971
PRIORITY APPLN. INFO.:
OTHER SOURCE(S):
GI A 19940208 US 1992-914837 US 1992-914837 19920716 19920716 MARPAT 121:35024

Title compds. I (R1 = R9CO(CHNR7R8)m(CH2)n wherein n = 1-3, m = 0,1, R7, R8 = H, C1-4 alkyl, R9 = HO, C1-4 alkowy, R8R7N; R3, R5 = Br, C1, iodo, Me; R31 = H, C1, Br, iodo, C1-4 alkyl, C4-6 cycloalkyl, C1-4 haloalkyl, C4-6 halocycloalkyl, Ar(R10)cH wherein Ar = 5-hydroxypyrid-27-3-yl, 6-hydroxypyrid-3-yl, 6-hydroxypyrid-3-yl, 6-hydroxypyridazin-3-yl, 6-methoxypyridazin-3-yl, 6-hydroxypyridazin-3-yl, 6-hydroxypyridazin-3-yl, R0-1-2-yl, R0

ANSWER 9 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)
L-Tyrosine, 3,5-diiodo-O-[4-methoxy-3-](4-methoxyphenyl)methyl]phenyl]-N(trifluoroacetyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

117896-25-0 CAPLUS L-Tyrosine, 0-[3-[(3-fluoro-4-methoxyphenyl]methyl]-4-methoxyphenyl]-3,5-diiodo-N-(trifluoroacetyl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

117896-26-1 CAPLUS L-Tyrosine, 3,5-diiodo-O-[4-methoxy-3-[(4-methoxy-3-methylphenyl)methyl]phenyl]-N-(trifluoroacetyl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

117896-27-2 CAPLUS L-Tycosine, 3,5-diiodo-O-{4-methoxy-3-[{4-methoxy-3-(1-methylathyl)phenyl]methyl]phenyl]-N-(trifluoroacetyl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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### Page 11

L4 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:115292 CAPLUS
110:115292 Selective thyromimetics. Cardiac-sparing thyroid hormone analogs containing 3'-acylmethyl substituents
Leeson, Paul D.; Emmett, John C.; Shah, Vuicendra P.; Showell, Graham A.; Novelli, Ricardor Prain, H. Douglass Benson, Martin G.; Ellis, David; Pearce, Nigel J.; Underwood, Anthony H.

CORPORATE SOURCE: Smith Kline French Res. Ltd., Frythe/Welwyn, AL6 9AR, UK

UX Journal of Medicinal Chemistry (1989), 32(2), 320-36 CODEN: JMCMAR; ISSN: 0022-2623 Journal English CASREACT 110:115292

DOCUMENT TYPE: LANGUAGE: OTHER SOURCE(S): GI

Introduction of specific arylmethyl groups at the 3'-position of the thyroid hormone 3,3',5'-triodo-L-thyronine [T3], and its known hormonally active derive., gives liver-selective, cardiac-sparing thyromimetics (e.g., 1, X = 0, 5; R = aryl group), with potential utility as plasma cholesterol lowering agents. Correlations between in vivo and in vitro receptor binding affinities show that liver/heart selectivity does not depend on receptor ecognition but on penetration or access to receptors in vivo. QSAR studies of the binding data of a series of 20 3'-arylmethyl T3 analogs show that electrones, groups at the para position increase both receptor binding and selectivity in vivo. However, increasing 3'-arylmethyl hydrophobicity increases receptor binding but reduces selectivity. Substitution at ortho and meta positions reduces both inding and selectivity. Neplacement of the 3,5-iod groups by halogen or Me maintains selectivity, with 3,5-dibromo analogs in particular having increased potency combined with oral bioavailability. Di-Ph thioether derivs. also have improved potency but are less orally active. At the 1-position, the D enantiomer creatins selectivity, but removal of the alpha-amino to give a propionic acid results in loss of selective thyromimetic activity.

105170-33-0P 117896-28-3P 117896-28-4P 117917-22-3P 117917-23-4P 117917-23-4P 117917-23-4P 117917-23-8P 117917-23-8P 117917-23-9P 117917-23-4P 117917-24-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREF (Preparation); PACT (Reactant) creagent) (prepn. and demethylation and hydrolysis of)

ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS

117896-28-3 CAPLUS L-Tyrosine, 3,5-diodo-0-[4-methoxy-3-[(2-methoxyphenyl)methyl]phenyl]-N-(trifluoroacetyl)-, ethyl ester (9CI) (CA INDEX NAME)

117896-29-4 CAPLUS L-Tyrosine, O-[3-[(3-chloro-4-methoxyphenyl)methyl]-4-methoxyphenyl]-3,5-diiodo-N-(trifluoroacetyl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

117917-22-3 CAPLUS L-Tycosine, 0-[3-[(4-cyanophenyl)methyl]-4-methoxyphenyl]-3,5-diiodo-N-(trifluoroacetyl)-, methyl ester (9CI) (CA INDEX NAME)

ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

117917-23-4 CAPLUS L-Tyrosine, J.5-diodo-O-[4-methoxy-3-[(4-nitrophenyl)methyl]phenyl]-N-(trifluoroacetyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

117917-24-5 CAPLUS L-Tyrosine, O-[3-[(4-fluorophenyl)methyl]-4-methoxyphenyl]-3,5-diiodo-N-(trifluoroacetyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

117917-26-7 CAPLUS L-Tyrosine, O-[3-[[4-(acetylamino)phenyl]methyl]-4-methoxyphenyl]-3,5-diodo-N-(trifluoroacetyl)-, methyl ester (9C1) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

117653-12-0 CAPLUS L-Tyrosine, O-[4-hydroxy-3-[(4-nitrophenyl)methyl]phenyl]-3,5-diiodo (9C1) (CA INDEX NAME)

117653-13-1 CAPLUS L-Tyrosine, O-[3-((4-aminophenyl)methyl]-4-hydroxyphenyl]-3,5-diiodo-,dihydrobromide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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117653-14-2 CAPLUS L-Tyrosine, O-[4-hydroxy-3-[(2-hydroxyphenyl)methyl]phenyl]-3,5-diiodo-(9CI) (CA INDEX NAME)

RN 117653-15-3 CAPLUS

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ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

105170-31-8P 117653-10-8P 117653-11-9P
117653-12-0P 117653-13-1P 117653-14-2P
117653-15-3P 117653-16-4P 117653-17-5P
117653-16-6P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. and thyromimetic activity of)
105170-31-8 CAPLUS
L-Tyrosine, O-{4-hydroxy-3-[(4-hydroxyphenyl)methyl]phenyl]-3,5-diiodo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

117653-10-8 CAPLUS L-Tyrosine, O-{3-{(4-cyanopheny1)methy1}-4-hydroxypheny1}-3,5-diiodo-(9C1) (CA INDEX NAME)

117653-11-9 CAPLUS L-Tytosine, O-[3-[(4-fluorophenyl)methyl]-4-hydroxyphenyl]-3,5-diiodo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)
L-Tyrosine, O-[3-[(3-fluoro-4-hydroxyphenyl]methyl]-4-hydroxyphenyl]-3,5diiodo- (9CI) (CA INDEX NAME)

117653-16-4 CAPLUS L-Tyrosine, O-[3-[(3-chloro-4-hydroxyphenyl)methyl]-4-hydroxyphenyl]-3,5-diodo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

117653-17-5 CAPLUS L-Tyrosine, O-[4-hydroxy-3-[(4-hydroxy-3-methylphenyl)methyl]phenyl]-3,5-diodo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

117653-18-6 CAPLUS L-Tyrosine, O-[4-hydroxy-3-[{4-hydroxy-3-(1-methylethyl)phenyl]methyl]phen yl]-1,5-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

6/23/2003

ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

72469-00-2 IT RL: BAC (Biological activity or effector, except adverse): BIOL

(Siological study)
(Siological study)
(Siological study)
(Chyromimetic activity of)
(7469-00-2 CAPLUS
L-Tyrosine, 0-[4-hydroxy-3-(phenylmethyl)phenyl]-3,5-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 11 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued) L-Tyrosine, N-acetyl-3,5-diiodo-0-[4-methoxy-3-(phenylmethyl)phenyl]-,ethyl ester (SCI) (CA NIOEX NAME)

Absolute stereochemistry.

111088-36-9 CAPLUS L-Tyrosine, N-acetyl-O-(3-benzoyl-4-methoxyphenyl)-3,5-diiodo-, ethylester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

111088-50-7 CAPLUS L-Tyrosine, 3,5-diiodo-O-[4-methoxy-3-(2-phenylethy1)phenyl]-N-ttifluoroacetyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 111087-79-7P 111088-00-7P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and thyromimetic activity of) 111087-79-7 CAPLUS

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L-Tyrosine, O-[4-hydroxy-3-(2-phenylethyl)phenyl]-3,5-diiodo- (9CI) (CA INDEX NAME)

Page 13

L4 ANSWER 11 OF 15
ACCESSION NUMBER:
DOCUMENT NUMBER:
108:38334 CAPLUS
108:38334 Thyroid hormone analogs. Synthesis of 3'-substituted
3,5-diodo-L-thyronines and quantitative
structure-activity studies of in vitro and in vivo
thyronimetic activities in rat liver and heart
Leeson, Paul D.: Ellis, David: Emmett, John C.: Shah,
Virendra P.: Showell, Graham A.: Underwood, Anthony H.
Source:
SOURCE:
DOCUMENT TYPE:
LANGUAGE:
OTHER SOURCE(S):
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CAPLUS COPPRIGHT 2003 ACS
1988:38334 CAPLUS
108:38334
Thyroid hormone analogs. Synthesis of 3'-substituted
3,5-diodo-L-thyronines and quantitative
structure-activities in rat liver and heart
Leeson, Paul D.: Ellis, David: Emmett, John C.: Shah,
Virendra P.: Showell, Graham A.: Underwood, Anthony H.
Sairk Kline French Res. Ltd., Frythe/Welvyn, AL6 9AR,
UK
Journal of Medicinal Chemistry (1988), 31(1), 37-54
CODEN: JNCMAR: ISSN: 0022-2623
Journal
DOCUMENT TYPE:
LANGUAGE:
CASREACT 108:38334

DOCUMENT TYPE: LANGUAGE: OTHER SOURCE(S): GI

Twenty-nine title compds. I (R = CH2:CH2, ally1, Bu, CH2CH2Ph, CH2OH, etc.) were prepd. by using established methods and by a new route involving manipulation of a 3'-formyl intermediate. In vitro hormone receptor binding (to intact nuclei) and in vivo thyromimatic activity (induction of mitochondrial 3-phosphoglycerate oxidoreductase, GPBI) were measured in rat liver and heart for these new analogs and for the 19 previously reported 3'-substituted 3.5-didoo-L-thyronines. Anal. of the binding date using theor. conformation and quant. structure-affinity methods implies that the 3'-substituent recognition site on the thyroid hormone receptor is hydrophobic and limited in depth to the length of the natural iodo substituent, but has sufficient width to accommodate a Ph or cyclohexyl group. Receptor binding is reduced by approx. 10-fold in 3'-acyl derivs. which form strong intramol. acceptor hydrogen bonds with the adjacent 4'-hydroxyl. The compds. showed no differences in their relative affinities for heart and liver nuclei, suggesting that receptors in these tissues are similar. However, the relationships between thyromimetic activity (induction of GPDH) and nuclear binding showed some tissue differences. A high correlation between activity and binding is obad. for full agonists in the heart, but an equally significant correlation for the liver data is only seen when 3'-substituent bulk (molar refractivity) is included in the anal. These results suggest the possibility that differential tissue penetration or access to receptors may occur in vivo.

may occur in vivo.

111088-02-9P 111088-36-9P 110089-50-7P
RL: RCT (Reactant); SFN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deblocking of)

111088-02-9 CAPLUS

L4 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2003 ACS Absolute stereochemistry. (Continued)

111088-00-7 CAPLUS L-Tyrosine, 0-(3-benzoyl-4-hydroxyphenyl)-3,5-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

72469-00-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(thyromimetic activity of)
72469-00-2 CAPLUS
L-Tyrosine, 0-[4-hydroxy-3-(phenylmethyl)phenyl]-3,5-diiodo-(9CI) (CA
INDEX NAME)

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1987:131516 CAPLUS DOCUMENT NUMBER: 106:131516

106:131516
A thyromimetic that decreases plasma cholesterol levels without increasing cardiac activity Underwood, A. H.: Emmett, J. C.: Ellis, D.: Flynn, S. B.: Leeson, P. D.: Benson, G. M.: Novelli, R.: Pearce, N. J.: Shah, V. P.
Smith Kline and French Res. Ltd., Welvyn/Hertfordshire, AL6 9AR, UK
Nature (London, United Kingdom) (1986), 324(6096), 425-9 TITLE: AUTHOR(S):

CORPORATE SOURCE:

SOURCE:

CODEN: NATUAS: ISSN: 0028-0836

DOCUMENT TYPE: English

A new class of thyromimetics (agents that mimic the ability of the thyroid hormone T3 [6893-02-3] to decrease plasma cholesterol levels) is described. The most potent of these SXF 194901 (1) [105211-23-2] (as deed. by the induction of mitochondrial cytochrome c 3-phosphoglycerate oxidoreductase [9001-49-4] in heart and liver of hypothyroid rats) was as active as T3 at reducing cholesterol levels and at stimulating liver function but had .apprx.0.1% the activity of T3 on heart function. In hypothyroid rats and rats with normal thyroid function, I was also shown to be a potent hypocholesterolemic agent with only a small effect on metabolic rate (detd. by whole body 0 consumption). The affinities of the thyromimetics for the thyroid hormone receptor of isolated heart and liver nuclei were detd., and the relationship between receptor affinity and structure is discussed.

72469-00-2 105170-31-9.

RL BIOL (Biological study)
(as thyromimetic, hypocholesterolemic activity of and heart and liver functions response to, thyroid hormone receptor binding in relation to) 72469-00-2 CAPLUS
L-Tyrozine. O-[4-hydroxy-3-(phenylmethyl)phenyl]-3,5-diiodo-(9CI) (CA AB

/2403-00-2 CAPLUS L-Tyrosine, 0-[4-hydroxy-3-(phenylmethyl)phenyl]-3,5-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:609386 CAPLUS
DOCUMENT NUMBER: 105:209386
THYCONIES AND ACS
INVENTOR(5): Leeson, Paul David: Emmett, John Colin: Underwood, Anthony Hubert: Ellis, David
PATENT ASSIGNEE(5): Smith Kline and French Laboratories Ltd., UK
EUL Pat. Appl., 59 pp.
CODEN: EPEXEW

DOCUMENTITYPE: Patent: 5
EANBUA ACC. NUM, COUNT: 1

English 1

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

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				FR, GB, I	T. LI	. 1	U. NL. SE		
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		577917		19881006					
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		77605	A1	19900209		IL	1986-818626 1986-77605	19860114	
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	DK	164592	С	19921207					
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	NO	B600159	A	19860721		NO	1986-159	19860117	
	HU	40401	A2	19861228		HU	1986-244	19860117	
	HU	194807	В	19880328					
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	JP	07103070	B4	19951108					
	CN	86100894	A	19860903		CN	1986-100894	19860118	
	CN	1010310	B A	19901107					
	US	4826876	A				1987-136240		
	US	4910305	A	19900320			1988-168780		
	US	5061798	A	19911029			1989-428264		
RIO	RIT	Y APPLN. I	NFO.:				95-1372		
							86-300178		
							6-818626		
							38-168780	19880316	
THE	R S	OURCE (S):	CZ	SREACT 105:	20936	36			

CASREACT 105:209386

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#### Page 14

ANSWER 12 OF 15 CAPLUS COPYRIGHT 2003 ACS

105170-31-8 CAPLUS L-Tycosine, 0-[4-hydroxy-3-[(4-hydroxyphenyl)methyl]phenyl]-3,5-diiodo-(9C1) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

105170-41-0 CAPLUS L-Phenylalanine, 3.5-diiodo-4-[[4-methoxy-3-[(4-methoxyphenyl]methyl]phenyl]thio]-N-(trifluoroacetyl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

105170-46-5 CAPLUS L-Tycosine, O-[4-hydroxy-3-[1-(4-hydroxyphenyl)ethyl]phenyl]-3,5-diiodo-N-(trifluoroacetyl)-, ethyl ester (9CI) (CA INDEX NAME)

ANSWER 13 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

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105170-31-8P 105170-36-3P 105170-42-1P
105170-47-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as anticholesteremic)
105170-31-8 CAPUS
L-Tyrosine, O-[4-hydroxy-3-[(4-hydroxyphenyl)methyl]phenyl]-3,5-diiodo(9CI) (CA INDEX NAME)

Absolute stereochemistry.

105170-36-3 CAPLUS
L-Phenylalanie, 4-[[4-hydroxy-3-{(4-hydroxyphenyl)methyl]phenyl]thio]-3,5-diiddo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

105170-42-1 CAPLUS L-Tyrosine, 0-[4-hydroxy-3-[1-[4-hydroxyphenyl]ethyl]phenyl]-3,5-diiodo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 14 OF 15
ACCESSION NUMBER:
DOCUMENT NUMBER:
1982:466791 CAPLUS
97:66791
Chemical structure-biological activity study of the thyroxine binding site of human prealbumin
AUTHOR(S):
Simon, Z.: Chiriac, A.: Chiriac, Veronica
Discipl. Biofix., Inst. Med., Timisoara, Rom.
Timisoara Medicala (1981), 26(3), 26-8
CODEN: TIMEBY: ISSN: 0493-3079. \*\*\* (2022)\*\*
DOCUMENT TYPE:
LANGUAGE:
Romanian

LANGUAGE: GI

The T4 (I) [51-48-9] receptor of human prealbumin was studied by the MTD method (Balaban, A. T., et al., 1980) based on binding data for 27 T4 derivs. (Andrea, T. A., et al., 1980). Min. steric differences were calcd. by a variant which allowed for differentation between atoms of the 2nd, 3rd, or higher periods. The structure activity relation with MTD and an indicator variant for the presence of an NI33 group gave the values of correlation coeff. r = 0.95 and std. deviation S = 0.71 kcal/mol. These values were in agreement with those obtained by the more complex method of G. M. Crippen (1980).
72469-00-2 RL: PROC (Process) (prealbumin binding of, in human, structure in relation to)
72469-00-2 CAPLUS
L-Tyrosine, 0-[4-hydroxy-3-(phenylmethyl)phenyl]-3,5-diiodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Habte

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L4 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)

105170-47-6 CAPLUS L-Tyrosine, N-acetyl-0-[4-hydroxy-3-[(4-hydroxyphenyl)methyl]phenyl]-3,5-diodo-[9C1] (CA INDEX NAME)



DOCUMENT TYPE: LANGUAGE: GI



The relative binding affinities to the human plasma protein prealbumin of the thyroid hormones, L-thyroxine (I) [51-48-9] and L-3,3',5-triidothyronine [II] [693-02-3], and of 37 close structural analogs were measured by equil. dialysis. Anal. of the contributions of substituents to binding showed that all 4 iodine atoms contribute favorably. Addn. of an iodine atom to an analog contribute more favorably in the outer ring than in the inner ring. Halogen substituents in the 3, 5, and 3' positions contributed more to binding than did alkyl groups with the same hydrophobic character in the same positions. This suggests a H-bonding and(or) charge transfer interaction between the halogen and the protein. An electrostatic interaction between the carboxylate ion of the hormone side chain and the ammonium ion of lysine-15 accounts for the obod. order in affinities: tetraprop [39846-93-0] > [I and D-thyroxine (51-49-0]) > thyroxamine [3571-49-1]. I bound with higher affinity than did D-thyroxine due to an interplay of electrostatic and steric forces involving the lysine-15, leucine-17, and valine-121 residues. The relative contributions of various structural features of the hormones in binding to prealbumin, I-binding globulin, and cat liver nuclear receptor were compared. Strong similarities were obod. In the features of the 3 and 5 positions and in the side chains in contributing binding affinity to prealbumin and to the receptor. Binding to I-binding globulin and to prealbumin and to the receptor. Binding to I-binding globulin and to prealbumin and to the receptor. Binding to I-binding globulin and to prealbumin and to the receptor. Binding to I-binding globulin and to prealbumin and to the receptor. Binding so I-binding globulin and to prealbumin and to the receptor. Binding to I-binding globulin and to prealbumin and to the receptor.

RL: PROC (Process)
(prealbumin binding of, structure in relation to)

6/23/2003

- L4 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2003 ACS (Continued)
  RN 72469-00-2 CAPLUS
  CN L-Tycosine, O-(4-hydroxy-3-(phenylmethyl)phenyl)-3,5-diodo- (9CI) (CA-INDEX NAME)

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